

# Dimension reduction via timescale separation

## in stochastic dynamical systems

Todd L. Parsons

*Laboratoire de Probabilités et Modèles Aléatoires, CNRS UMR 7599, Université Pierre et Marie Curie, Paris, 75005, France.*

Tim Rogers

*Centre for Networks and Collective Behaviour, Department of Mathematical Sciences, University of Bath, Bath, BA2 7AY, UK.*

We review the development and applications of a systematic framework for dimension reduction in stochastic dynamical systems that exhibit a separation of timescales. When a multidimensional stochastic dynamical system possesses quantities that are approximately conserved on short timescales, it is common to observe on long timescales that trajectories remain close to some lower-dimensional subspace. Here, we derive explicit and general formulae for a reduced-dimension description of such a process that is exact in the limit of small noise and well-separated slow and fast dynamics. The Michaelis-Menten law of enzyme-catalyzed reactions is explored as a worked example. Extensions of the method are presented for infinite dimensional systems and processes coupled to general noise sources.

### I. INTRODUCTION

An unfortunate truth not often acknowledged clearly enough in our teaching is that the overwhelming majority of mathematical models cannot be solved. Most variables are not separable, most functions do not have elementary antiderivatives, most polynomial roots are not expressible with radicals, and so on. Despite this, we still believe in the power of mathematics as a tool for the investigation of natural phenomena.

Justification for this belief is found in the interaction of theoretical and experimental physics, where the predictions of mathematical models are routinely found to be exquisitely accurate. One important reason for this “unreasonable effectiveness” of mathematics (Wigner, 1960) is that physical systems often enjoy gigantic separation of scales, meaning that a process of interest may be treated (indeed, modelled) separately from what is happening at other spatial or temporal scales. Here ‘separate’ does not have to mean ‘in isolation’, as the effects of the unmodelled scales may be effectively incorporated in a physical model as random noise. The example everyone knows is Brownian motion. The unpredictable motion of the pollen grain is driven by many small interactions with water molecules; rather than attempt to actually model the position of each water

molecule, we make a heroic leap of imagination and substitute for the water a series of independent random ‘kicks’. The resulting theory is sufficiently simple that the motion of the pollen grain can now be completely understood and predicted (in a statistical sense at least).

Gathering up the effects of large numbers of interacting particles into a single simple noise term may sound reckless at first, but in fact it can be precisely justified in a broad range of circumstances (Kurtz, 1978; van Kampen, 1992). This methodology is now readily applied to problems in biology, finance, sociology, and many other fields. However, mathematical modellers in these areas have not yet come close to the same levels of predictive success achieved in physics. There are two intertwined issues: the first is the ability of an appropriately formulated mathematical model to capture the essential behaviours of the system of interest; the second is our ability to ‘solve’ said model to extract quantitative predictions and qualitative understanding. Often, the separation of scales in, for example, a biological system is not so obvious and therefore more degrees of freedom must be included in the model to achieve an acceptable representation of reality. This then has a knock-on effect for the analysis of the model as higher-dimensional systems tend to be harder to work with, both analytically and in simulations.

All is not lost, however; although a separation of timescales may not be obvious at the stage of writing a model, it can still play an important role in its analysis. Recently several groups have independently found a natural separation of scales emerging in ecological models (Chotibut and Nelson, 2015; Constable and McKane, 2014b, 2015; Constable et al., 2013; Durrett and Popovic, 2009; Lin et al., 2012; Parsons, 2012; Parsons and Quince, 2007; Parsons et al., 2008, 2010; Pigolotti and Benzi, 2014; Rogers et al., 2012a,b). Loosely speaking, it is often the case that the total size of a population varies much more rapidly than its composition. This is a kind of timescale separation that cannot be put by hand into a model as there is a complex feedback between the fast and slow degrees of freedom, which must be carefully computed. Mathematically, this is not straightforward, and a host of different strategies have previously been employed to approximate the effects of this feedback between scales. A rigorous treatment of this situation can in fact be found in (Katzenberger, 1991) and (Funaki and Nagai, 1993), however, the results of these works are difficult to apply in practice as they lack explicit formulations of certain key quantities. Our purpose here is to synthesise the various methods of the above mentioned authors with the rigorous theory of Katzenberger, and distil into a single robust, systematic and provably correct procedure for timescale separation, which we believe will be of considerable general use. The main results are contained in Section III, where we describe a map from a high-dimensional system of equations (1) to a lower-dimensional one (2), via explicit formulae that are summarised in Table I.

The general setting for our calculations will be models expressed as coupled stochastic differential equations, with some small parameter  $\varepsilon$  that controls the separation of timescales. We are particularly interested in systems that are derived from a complex underlying interacting process, so that the noise terms are *intrinsic*, representing the cumulative random effects of many interactions. Importantly in this case the noise, although non-negligible in its effect, is typically small in amplitude<sup>1</sup>. Three example application areas are: (i) cell behaviour (e.g. gene regulation), where small copy numbers imply noise but homeostasis suggests timescale separation (Ball et al., 2006), (ii) evolutionary models where noise arising from demographic fluctuations can alter the course of selection (references above), (iii) dynamical networks which are naturally extremely high-dimensional systems in need of low-dimensional proxies (Rogers and Gross, 2013).

In addition to the general theory outlined in Section III, we present in Section IV some worked examples and variations to the method. As a prototypical example of the standard method, we work through the derivation of a stochastic form of the Michaelis-Menten law for enzyme-catalysed reactions. The second example demonstrates the extension of the methods to an infinite dimensional setting. We then discuss the generalisation of the noise sources (for example to jump processes) and alternative characterisations of the diffusion process on the manifold. Before presenting the method itself, we give a very brief history of notable developments in stochastic timescale separation.

## II. LITERATURE

As mentioned above, the canonical example of timescale separation in physics is Brownian motion; stochastic interactions with the water molecules cause changes to the *velocity* of the pollen grain on a fast timescale, which have a cumulative effect of perturbing the *position* on a slower timescale. The process of moving from a description of the particle's motion in terms of position and velocity to one concerned just with position (thus reducing the dimension of the model from two to one) is known as *adiabatic elimination*<sup>2</sup>. Following the introductory discussion in (Gardiner et al., 1985), one may write equations of motion for the pollen grain of the form of Langevin equations such as

$$\frac{dx}{dt} = v, \quad m \frac{dv}{dt} = -v + \sqrt{\mu} \eta(t),$$

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<sup>1</sup> A complementary branch of theory exists dealing with the relaxation of this assumption, see (Arnold and Imkeller, 1998; Roberts, 2008) for starting points in the literature

<sup>2</sup> Also *fast variable elimination*, *fast mode elimination*, the *quasi-static approximation*, and many other alternatives.

where  $m$  is the mass,  $\mu$  a constant derived from the temperature of the water bath, and  $\eta(t)$  is Gaussian white noise. If the mass  $m$  is very small, we might approximate  $m \approx 0$  and thus  $v \approx \sqrt{\mu} \eta(t)$ . From this we derive the reduced description

$$\frac{dx}{dt} = \sqrt{\mu} \eta(t).$$

A reader encountering arguments of this type for the first time is likely to be suspicious, and rightly so. Although provably exact for the simple case described here, taking limits in a brusque fashion like this is generally inadvisable when dealing with stochastic dynamical systems. Nonetheless, the method is quite powerful and the same basic principle has been developed to various levels of rigour and generality by many authors, most notably Haken ([Haken and Wunderlin, 1982](#)).

Although conceptually appealing, the Langevin-style description of a stochastic system in terms of dynamical equations with noise hides some important complications. As any introductory text will warn, when writing such an equation we must specify the sense in which we are to understand the noise term  $\eta(t)$ . This choice then impacts the behaviour of the system under certain limits or changes of variables, potentially complicating the process of timescale separation. An alternative description of a stochastic system that avoids this ambiguity is in terms of a PDE describing the time evolution of the probability density, known as the Fokker-Planck Equation (also, the Kolmogorov forward equation). Timescale separation in this setting amounts to integrating out one or more degrees of freedom from the PDE to reduce its dimension. Physicists might understand this process through its natural analogue in quantum mechanics, the Born-Oppenheimer approximation ([Born and Oppenheimer, 1927](#)). In most applications the Fokker-Planck equation will not be exactly separable, necessitating the application by hand of a carefully chosen projection operator, an approach going back to the work of Zwanzig ([Zwanzig, 1960](#)).

Existing in parallel with the development of adiabatic elimination techniques in physics is a separate body of literature concerned with probabilistic models of biological processes that also exhibit a separation of timescales. This thread begins with early work on the convergence of Markov chains — particularly those appearing in genetics — to diffusion processes ([Feller, 1951](#); [Trotter, 1958](#)). Analyzing the Wright-Fisher model of allele frequencies in a population of large size  $N$ , Feller used the standard convention of measuring the population in units of  $N$  individuals (so one individual has weight  $\frac{1}{N}$ ), but rather than truncating the master equation by discarding terms of order  $\frac{1}{N^2}$  and greater, he also rescaled to a “slow time” so that  $\Delta t = \frac{1}{N}$ , which led to a well defined limit as  $N \rightarrow \infty$ , a procedure proved rigorously by Trotter.

Mathematical population genetics also provides an important early example of a stochastic

process explicitly considered at multiple timescales. In (Ethier and Nagylaki, 1980; Nagylaki, 1980), models of diploid populations with non-overlapping generations and geographic structure were analysed by separating a fast timescale on which, for example, the genotype frequencies would rapidly equilibrate to Hardy-Weinberg proportions, from a slow timescale over which allele frequencies would vary due to mutation and genetic drift. Their approach, obtained by an extension of the semi-group methods of (Trotter, 1958), requires the explicit characterization of infinite-dimensional spectral projection operators, and an explicit separation of the process into fast and slow variables, the former of which must be effectively constant on the slow-timescale. These requirements somewhat limit the generality of the approach, but it does have the virtue of being applicable to Markov processes other than Brownian motion, such as measure-valued processes (Harris et al., 2015).

Slightly over a decade later, two very general papers appeared that used similar approaches based in stochastic differential equations and classical, deterministic formulations of time-scale separation. The first, (Katzenberger, 1991), considered processes taking values in  $\mathbb{R}^d$ , but with a very general approach to stochastic noise, so that the results can be applied both to diffusion processes and discrete Markov processes (see the discussion in section IV.C), whilst the latter (Funaki and Nagai, 1993), allows the process to be defined on a general Riemann manifold  $M$ , but requires the noise to be the canonical Brownian motion on the manifold (see section IV.D). In both, there is a fast timescale on which the process essentially behaves like a deterministic dynamical system, with trajectories that approach a lower-dimensional “slow manifold”  $\Gamma$ . On the slow time-scale, the process is asymptotic to a diffusion process that is confined to the manifold  $\Gamma$ . Katzenberger characterized the diffusion on the slow manifold via stochastic differential equations and a function  $\pi$  (defined formally below), which, given an initial point  $\mathbf{x}$ , gives the point in  $\Gamma$  to which it will be carried by the fast dynamics, whereas (Funaki and Nagai, 1993) used the backward equation to describe the diffusion.

Unfortunately, in spite of their generality, (Katzenberger, 1991) and (Funaki and Nagai, 1993) have been frequently overlooked, as was the follow up (Funaki, 1995), where the problem of dimension reduction in infinite dimensions was considered for an SPDE of Ginzburg-Landau type. Indeed, special cases have been subsequently rediscovered. This is perhaps because, whilst these papers have the virtue of providing rigorous proofs, they are not necessarily useful for the practitioner: (Katzenberger, 1991) supposes the function  $\pi$  is given, whereas in applications it is frequently difficult or impossible to obtain in closed form, as the fast system may not be solvable. (Funaki and Nagai, 1993) gives a closed expression for the diffusion equation, though one that, except in the

case when the fast system is a gradient flow, requires extensive calculations with Fermi coordinates (like Katzenberger's  $\boldsymbol{\pi}$ , these are often impossible to obtain in closed form) and only applies when the noise is Brownian motion.

In what follows we will review the technique of Katzenberger from a application-driven perspective, providing a complete characterization of the reduced dimension process in the most general case and without assuming knowledge of the trajectories of the fast system.

### III. SLOW-MANIFOLD REDUCTION

We consider stochastic differential equations of the general type

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}) + \varepsilon \mathbf{h}(\mathbf{x}) + \sqrt{\mu} \mathbf{G}(\mathbf{x}) \boldsymbol{\eta}(t), \quad (1)$$

where the state variable  $\mathbf{x} = (x_1, \dots, x_d)^T \in \mathbb{R}^d$  is an  $d$ -dimensional vector, and there are  $s$  independent Itô white noise sources  $\boldsymbol{\eta}(t) = (\eta_1(t), \dots, \eta_s(t))^T$ . The vector-valued functions  $\mathbf{f} : \mathbb{R}^d \rightarrow \mathbb{R}^d$  and  $\mathbf{h} : \mathbb{R}^d \rightarrow \mathbb{R}^d$  are the ‘outer’ and ‘inner’ parts of the drift respectively, and the matrix valued function  $\mathbf{G} : \mathbb{R}^d \rightarrow \mathbb{R}^{d,s}$  specifies the coupling of state variables to noise sources. We assume throughout that  $\mathbf{f}$  is twice differentiable, but place no constraints on the other functions. The parameters  $\varepsilon$  and  $\mu$  determine the separation of timescales and the strength of the noise.

We are interested in the case when  $\varepsilon$  and  $\mu$  are small and  $\mathbf{f}$  possesses a  $m$ -dimensional manifold of equilibria  $\Gamma \subset \mathbb{R}^d$  such that  $\mathbf{f}(\mathbf{z}) = \mathbf{0}$  for all  $\mathbf{z} \in \Gamma$ . We assume that this manifold is unique, connected, and globally attractive; then we expect solutions of (1) to rapidly approach and remain very close to  $\Gamma$ . In fact, it can be shown that the trajectories of  $\mathbf{x} \in \mathbb{R}^d$  converge those of a stochastic variable  $\mathbf{z} \in \Gamma$  with dynamics

$$\frac{d\mathbf{z}}{dt} = \varepsilon \mathbf{P}(\mathbf{z}) \mathbf{h}(\mathbf{z}) + \mu \mathbf{g}(\mathbf{z}) + \sqrt{\mu} \mathbf{P}(\mathbf{z}) \mathbf{G}(\mathbf{z}) \boldsymbol{\eta}(t), \quad (2)$$

where  $\mathbf{P}$  is a certain projection matrix derived from  $\mathbf{f}$ , and  $\mathbf{g}$  is a new contribution to the drift arising from the way in which fluctuations away from the manifold are suppressed. The derivation of this result and of explicit expressions for  $\mathbf{P}$  and  $\mathbf{g}$  follows. Readers with a specific problem in mind may wish to jump straight to the appropriate result, which can be found by referring to Table I.

Before moving on with the derivation, a couple of comments are necessary. An equivalent formulation of equation (1) more common in the mathematical literature reads

$$d\mathbf{x} = (\mathbf{f} + \varepsilon \mathbf{h}) dt + \sqrt{\mu} \mathbf{G} d\mathbf{W}_t, \quad (3)$$

Case	Procedure
Outer system ( $\varepsilon = \mu = 0$ ) is solvable	Use equations (4, 5) and (9, 10)
Manifold is one-dimensional	Use equations (10) and (15, 16)
Manifold is $m$ -dimensional	Use equations (10) and (17 – 21)

TABLE I Quick reference table of equations applying to different cases of slow-manifold reduction.

where  $\mathbf{W}_t$  is an  $s$ -dimensional Weiner process. Our results apply to either version, but here we prefer the physics notation using white noise  $\boldsymbol{\eta}(t)$  primarily because we wish to appeal to intuition coming from deterministic dynamical systems. The corresponding deterministic analysis comprises a large body of work known as *Center Manifold Theory*. Here we only scratch the surface of this field; the interested reader is referred to (Wiggins, 2003). One important difference for us is that the deterministic theory is usually developed in the neighbourhood of an isolated fixed point of the dynamics, whereas we are concerned with behaviour of the stochastic system near an attractive surface. This view is necessary since the stochastic nature of reduced model means that it may wander very far from its starting point, and thus a local description is no longer appropriate. A consequence of this is that we will not be making use of coordinate transformations (a standard tool of the deterministic theory) for the simple reason that we would in principle require a different transformation at each point in space, complicating the analysis enormously.

Examining our model (1) when  $\varepsilon$  and  $\mu$  are small, one might imagine a picture in which the state of the system is quickly carried onto the manifold by the fast outer drift term  $\mathbf{f}$ . Following this fast initial transient, it may then receive multiple stochastic ‘kicks’ carrying it away from the manifold, each time only to return again via the paths described by  $\mathbf{f}$ . See Figure 1 for an illustrative example. This intuition can be made concrete by considering the flow map of the outer system. Define

$$\phi_t(\mathbf{x}) = \boldsymbol{\xi}(t), \quad \text{where } \boldsymbol{\xi}(t) \text{ solves } \frac{d\boldsymbol{\xi}}{dt} = \mathbf{f}(\boldsymbol{\xi}), \quad \boldsymbol{\xi}(0) = \mathbf{x}. \quad (4)$$

Since the center manifold is globally attractive, all flow maps lead eventually to  $\Gamma$ . We write

$$\boldsymbol{\pi}(\mathbf{x}) = \lim_{t \rightarrow \infty} \phi_t(\mathbf{x}) \quad (5)$$

for the ‘landing point’ on the manifold of the trajectory starting at the point  $\mathbf{x}$ . Recalling that  $\mathbf{x}$  is random variable governed by equation (1), we introduce  $\mathbf{z} = \boldsymbol{\pi}(\mathbf{x})$ , which is also a random

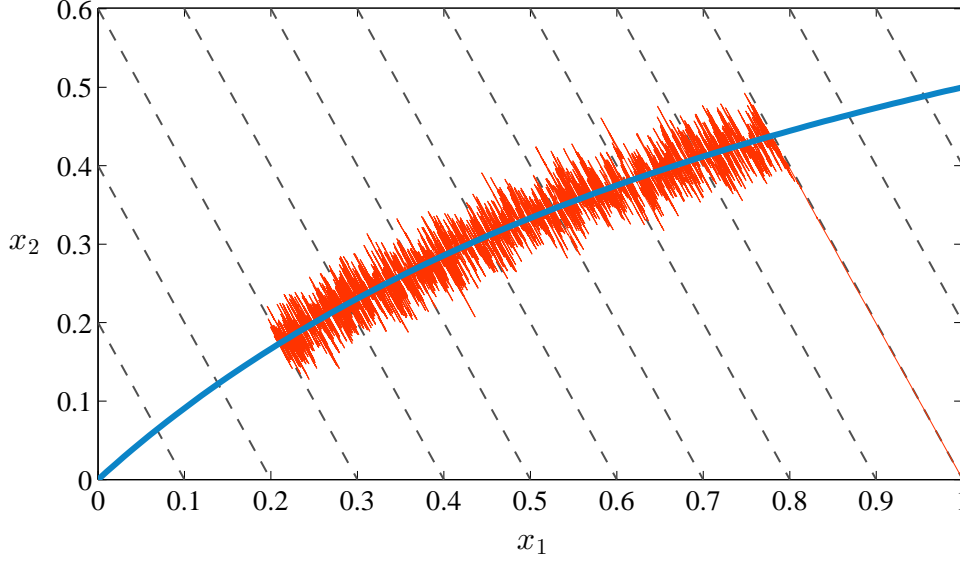


FIG. 1 **Thin Red:** Simulation of a single stochastic trajectory of an SDE of the type (1), with  $\mathbf{f}$ ,  $\mathbf{h}$  and  $\mathbf{G}$  corresponding to the Michaelis-Menten model (30, 31). **Thick Blue:** The slow manifold for this system, which the stochastic trajectory stays close to after the fast initial transient carrying it away from the initial condition (1,0). **Dashed Black:** The flow field of the outer drift term  $\mathbf{f}$ , to which the fast motion is approximately parallel.

variable. Application of Itô's formula (Itô, 1974) gives an evolution equation for  $\mathbf{z}$ :

$$\begin{aligned} \frac{dz_i}{dt} &= \sum_j \frac{\partial \pi_i}{\partial x_j} \frac{dx_j}{dt} + \frac{\mu}{2} \sum_{s,j,k} G_{js}(\mathbf{x}) G_{ks}(\mathbf{x}) \frac{\partial^2 \pi_i}{\partial x_j \partial x_k} \\ &= \sum_j \frac{\partial \pi_i}{\partial x_j} \left( f_j(\mathbf{x}) + \varepsilon h_j(\mathbf{x}) \right) + \frac{\mu}{2} \sum_{s,j,k} G_{js}(\mathbf{x}) G_{ks}(\mathbf{x}) \frac{\partial^2 \pi_i}{\partial x_j \partial x_k} + \sqrt{\mu} \sum_{s,j} G_{js}(\mathbf{x}) \frac{\partial \pi_i}{\partial x_j} \eta_s(t). \end{aligned} \quad (6)$$

Note that since it is the endpoint of the trajectory as  $t \rightarrow \infty$ ,  $\boldsymbol{\pi}(\boldsymbol{\xi}(t)) \equiv \boldsymbol{\pi}(\mathbf{x})$  for all  $t$ . Thus,

$$0 = \left. \frac{d}{dt} \right|_{t=0} \pi_i(\boldsymbol{\xi}(t)) = \sum_j \frac{\partial \pi_i}{\partial x_j} \left. \frac{d\xi_j}{dt} \right|_{t=0} = \sum_j \frac{\partial \pi_i}{\partial x_j} f_j(\mathbf{x}) \quad (7)$$

and the order 1 term in (6) vanishes.

In the limit of small  $\varepsilon$  and small  $\mu$  it was shown by Katzenberger (Katzenberger, 1991) that, after a fast initial transient,  $\mathbf{x}$  stays in a neighbourhood of  $\Gamma$  with high probability. We are thus motivated to suppose  $\mathbf{x} \approx \mathbf{z}$  and hence to replace  $\mathbf{x}$  with  $\mathbf{z}$  everywhere in the right hand side of equation (6). We obtain the closed expression

$$\frac{dz_i}{dt} = \varepsilon \sum_j P_{ij}(\mathbf{z}) h_j(\mathbf{z}) + \frac{\mu}{2} \sum_{s,j,k} G_{js}(\mathbf{z}) G_{ks}(\mathbf{z}) Q_{ijk}(\mathbf{z}) + \sqrt{\mu} \sum_{s,j} P_{ij}(\mathbf{z}) G_{js}(\mathbf{z}) \eta_s(t), \quad (8)$$

where  $\mathbf{P}$  is a matrix and  $\mathbf{Q}$  an array defined by

$$P_{ij}(\mathbf{z}) = \left. \frac{\partial}{\partial x_j} \pi_i(\mathbf{x}) \right|_{\mathbf{x}=\mathbf{z}}, \quad Q_{ijk}(\mathbf{z}) = \left. \frac{\partial^2}{\partial x_j \partial x_k} \pi_i(\mathbf{x}) \right|_{\mathbf{x}=\mathbf{z}}. \quad (9)$$



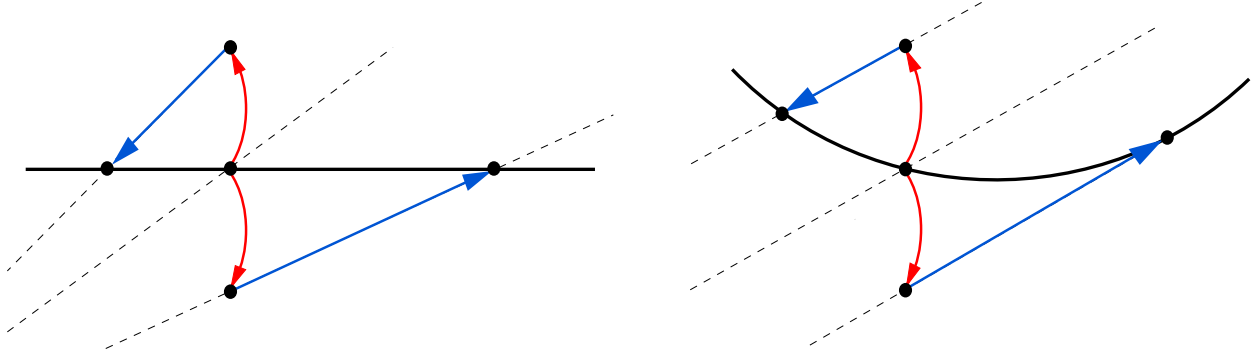


FIG. 2 **Left:** Here, the variation in the angle between the fast (dashed) and slow (solid) subspaces creates a bias in the location of the return to the manifold of a perturbation away from it; an upward perturbation returns quite close on the left of the origin, but an equally likely downward perturbation is carried far to the right. **Right:** The same effect also occurs as a result of curvature of the manifold. In this figure the flow fields are parallel, but the manifold curves, resulting in the same rightwards bias in the projected system.

Equivalently we may rewrite (8) as equation (2), where the additional drift term is

$$\mathbf{g}(\mathbf{z}) = (\mu/2) \sum_{s,j,k} G_{js}(\mathbf{z}) G_{ks}(\mathbf{z}) Q_{ijk}(\mathbf{z}). \quad (10)$$

From the discussion above it may seem that it is necessary to have an analytic expression for the flow field  $\phi_t$  and its limit  $\pi$ , something which for many applications will not be possible. We see from definition (9), however, that in fact we are only required to compute the expansion of  $\pi$  up to second order in the neighbourhood of the manifold. The projection matrix  $\mathbf{P}(\mathbf{z})$  is entirely determined by the first order terms of this expansion, and typically it can be straightforwardly reconstructed from knowledge of the eigenvectors of the Jacobian matrix of  $\mathbf{f}$ , see Section III.B below. The calculation of the noise-induced drift term is more complicated, having contributions from two possible sources: variation of the alignment of the flow field, and curvature of the manifold. Both of these mechanisms can induce a bias in the direction of flow of the reduced dimension system, as illustrated in Figure 2. Before giving a general treatment we develop intuition by tackling a perturbation expansion which is exactly solvable for one-dimensional manifolds.

### A. One-dimensional manifolds

Consider a one-dimensional slow manifold described by a curve  $\gamma$ , parametrised using one of the spatial coordinates  $x_i$  so that  $\mathbf{x} = \gamma(x_i)$  on the manifold. In this setting our reduced dimension description (2) has only one degree of freedom; the most sensible choice is to focus on the  $i^{\text{th}}$  coordinate as this is the parametrisation we chose for the manifold. The dynamics of  $z_i$  follow (8)

under the substitution  $\mathbf{z} = \gamma(z_i)$ .

To compute the partial derivatives of  $\pi_i$  in the neighbourhood of the manifold, we develop a second-order perturbation theory. Consider a point  $\mathbf{x} = \gamma(z_i)$  on the manifold; clearly  $\pi(\mathbf{x}) = \gamma(z_i)$ . We make a small perturbation  $\mathbf{x} \mapsto \mathbf{x} + \Delta\mathbf{x}$ , and ask what perturbation  $z_i \mapsto z_i + \Delta z_i$  is required so that  $\pi(\mathbf{x} + \Delta\mathbf{x}) = \gamma(z_i + \Delta z_i)$ . Noting that  $\pi_i(\mathbf{x}) = z_i$ , we expand to second order

$$\Delta z_i = \sum_j P_{ij} \Delta x_j + \frac{1}{2} \sum_{j,k} Q_{ijk} \Delta x_j \Delta x_k + \dots \quad (11)$$

Near  $\mathbf{x}$  we can approximate the local action of the flow field by a linear projection in which all fast directions vanish immediately. For each  $z_i$  let  $\mathbf{v}(z_i)$  be a vector that is orthogonal to all of the  $n - 1$  fast directions at that point. The equation we must solve is thus

$$(\mathbf{x} + \Delta\mathbf{x} - \gamma(z_i + \Delta z_i)) \cdot \mathbf{v}(z_i + \Delta z_i) = 0. \quad (12)$$

In words, this equation demands that the perturbed point  $\mathbf{x} + \Delta\mathbf{x}$  lies in (the linear approximation to) the preimage of  $\pi$  at  $z_i + \Delta z_i$ . See Figure 3 for an illustration. To find the vector-valued function  $\mathbf{v}$  for a given system, we note that if  $\mathbf{J}(z_i)$  is the Jacobian of  $\mathbf{f}$  at the point  $\mathbf{x} = \gamma(z_i)$ , then typically  $\mathbf{v}(z_i)$  is the left eigenvector of  $\mathbf{J}(z_i)$  corresponding to the eigenvalue zero.

The series (11) allows us to develop both  $\gamma$  and  $\mathbf{v}$ :

$$\begin{aligned} \gamma_l(z_i + \Delta z_i) &= x_l + \gamma'_l \left( \sum_j P_{ij} \Delta x_j + \frac{1}{2} \sum_{j,k} Q_{ijk} \Delta x_j \Delta x_k \right) \\ &\quad + \frac{1}{2} \gamma''_l \left( \sum_{j,k} P_{ij} P_{ik} \Delta x_j \Delta x_k \right) \\ v_l(z_i + \Delta z_i) &= v_l + v'_l \left( \sum_j P_{ij} \Delta x_j + \frac{1}{2} \sum_{j,k} Q_{ijk} \Delta x_j \Delta x_k \right), \end{aligned} \quad (13)$$

where on the right we have dropped the argument  $(z_i)$  from  $\gamma$ ,  $\mathbf{v}$ ,  $\mathbf{P}$  and  $\mathbf{Q}$  to reduce clutter. Inserting these into the orthogonality equation (12) and collecting first-order terms gives

$$\sum_j \Delta x_j v_j - \sum_j \gamma'_j v_j \sum_k P_{ik} \Delta x_k = 0 \quad (14)$$

for all  $j$ . Since  $\Delta\mathbf{x}$  was arbitrary, we conclude

$$P_{ij} = \frac{v_j}{\sum_k \gamma'_k v_k}. \quad (15)$$

For the second order terms we find, after some rearrangement,

$$Q_{ijk} = \frac{1}{\sum_l \gamma'_l v_l} \left( v'_j P_{ik} + v'_k P_{ij} - P_{ij} P_{ik} \sum_l (2\gamma'_l v'_l + \gamma''_l v_l) \right). \quad (16)$$

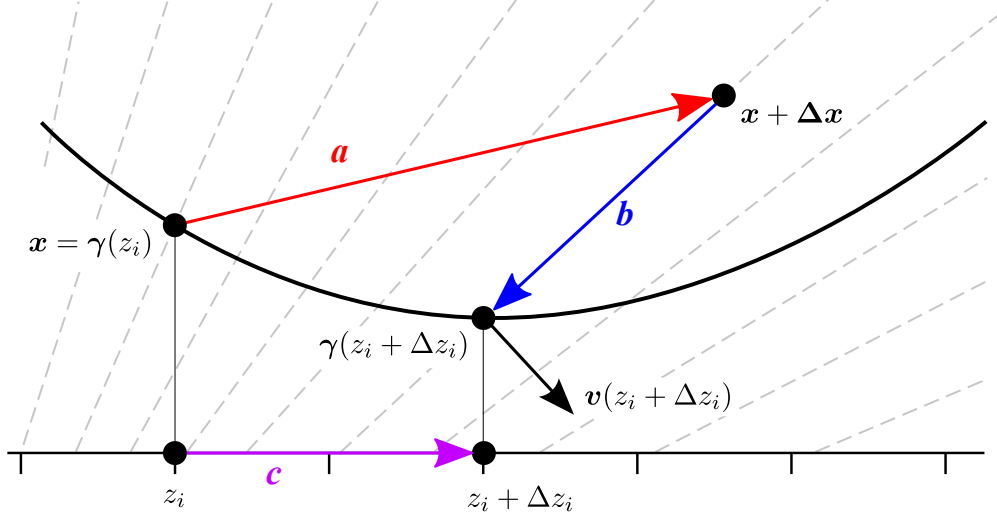


FIG. 3 Illustration of the perturbation expansion for a one-dimensional manifold, shown here as the thick black curve. A system initially specified by a point  $\mathbf{x} = \gamma(z_i)$  on the manifold receives a stochastic ‘kick’  $\Delta \mathbf{x}$  that carries it away along vector  $\mathbf{a}$ . The fast relaxation to back to the manifold follows the flow field, which is approximated by the straight line of vector  $\mathbf{b}$ . The new location on the manifold is  $\gamma(z_i + \Delta z_i)$ , where  $\Delta z_i$  is an inferred perturbation to  $z_i$ , illustrated here as vector  $\mathbf{c}$ . To determine this perturbation, we note that  $\mathbf{b} = (\mathbf{x} + \Delta \mathbf{x} - \gamma(z_i + \Delta z_i))$ , must align with the fast direction at the new manifold location, so must be perpendicular to the vector  $\mathbf{v}(z_i + \Delta z_i)$ . This is the content of equation (12).

Written this way, the separate contributions from variation of the flow field (terms involving  $\mathbf{v}'$ ) and curvature of the manifold (the  $\gamma''$  term) are clearly visible.

In higher dimensions, the above perturbation expansion is less useful, as it produces a larger system of equations which lacks an explicit solution. A different line of attack is necessary.

## B. Higher-dimensional manifolds

If the linearisation of the flow field  $\phi_t$  is known in the neighbourhood of the manifold then  $\mathbf{P}$  can be reconstructed easily. Specifically, around a point  $\mathbf{z} \in \Gamma$  the state space  $\mathbb{R}^d$  can be decomposed into a product of ‘slow’ and ‘fast’ subspaces of dimension  $m$  and  $d - m$ , respectively. The slow subspace is the tangent plane to the manifold at the given point; a perturbation in one of these directions is unaffected by the action of  $\mathbf{f}$ . Conversely, the fast subspace comprises perturbation directions that collapse quickly back to the manifold. The projection matrix  $\mathbf{P}(\mathbf{z})$  acts as the identity on the slow subspace and as zero on the fast subspace.

Unfortunately, no such simple formulation is available for  $\mathbf{Q}(\mathbf{z})$  in general. This problem was explored in (Parsons, 2012), where the following method was developed. This result is explained

fully in Appendix A, for now we simply present the computational steps.

Procedure for calculating  $\mathbf{P}$  and  $\mathbf{Q}$  at a point  $\mathbf{z} \in \Gamma$

1. Compute the Jacobian  $\mathbf{J}$  and diagonalize it, writing

$$\mathbf{J} = \mathbf{W}\mathbf{\Lambda}\mathbf{W}^{-1}. \quad (17)$$

where  $\mathbf{W} = (\mathbf{w}_1 \cdots \mathbf{w}_n)$  is a matrix of eigenvectors forming a basis of  $\mathbb{R}^d$ , with the  $m$  slow directions written first.  $\mathbf{\Lambda}$  is a diagonal matrix of eigenvalues with  $\lambda_1 = \cdots = \lambda_m = 0$  and  $\text{Re}(\lambda_{m+1}), \dots, \text{Re}(\lambda_n) < 0$ . Also compute the pseudo-inverse

$$\mathbf{J}^+ = \mathbf{W}\mathbf{\Lambda}^+\mathbf{W}^{-1}, \quad (18)$$

$$\text{where } \lambda^+ = \begin{cases} 0 & \text{if } \lambda = 0 \\ 1/\lambda & \text{if } \lambda \neq 0. \end{cases}$$

2. For each  $i$ , compute the Hessian  $\mathbf{H}_i$  defined by

$$H_{ijk} = \left. \frac{\partial f_i(\mathbf{x})}{\partial x_j \partial x_k} \right|_{\mathbf{x}=\mathbf{z}}.$$

Then find the solution  $\mathbf{X}_i$  of the Lyapunov equation

$$\mathbf{J}^T \mathbf{X}_i + \mathbf{X}_i \mathbf{J} = -\mathbf{H}_i. \quad (19)$$

NB: this is a linear problem that is straightforwardly solved ([Bartels and Stewart, 1972](#)).

3. Finally, the projection matrix is given by

$$\mathbf{P} = \mathbf{I} - \mathbf{J}^+ \mathbf{J}. \quad (20)$$

and for  $\mathbf{Q}$  we have

$$Q_{ijk} = \sum_l -J_{il}^+ [\mathbf{P}^T \mathbf{H}_l \mathbf{P}]_{jk} + P_{il} [\mathbf{X}_l - \mathbf{J}^{+T} \mathbf{H}_l \mathbf{P} - \mathbf{P}^T \mathbf{H}_l \mathbf{J}^+]_{jk}. \quad (21)$$

## IV. EXAMPLES AND VARIATIONS

### A. Simple example: Michaelis-Menten kinetics

The Michaelis-Menten law is perhaps one of the most widely-applied examples of timescale separation. It is a model for the net rate of production in a chemical reaction that is catalysed by

an enzyme, in which it is assumed that the process of enzyme binding and unbinding occurs very much faster than the catalytic reaction of interest. Using the notation of chemical reactions, one may write



where  $E$  symbolises the enzyme,  $S$  the substrate,  $C$  the enzyme-substrate complex, and  $P$  the product. The parameters  $k_f$  and  $k_r$  give the rate of binding (forward) and unbinding (reverse) of the enzyme to the substrate, while  $k_{\text{cat}}$  specifies the rate of catalysis.

Assuming the reaction takes place in a domain of infinite volume, one may write the deterministic equations

$$\begin{aligned} \frac{dS}{dt} &= -k_f ES + k_r C, \\ \frac{dE}{dt} &= -k_f ES + (k_r + k_{\text{cat}})C, \\ \frac{dC}{dt} &= k_f ES - (k_r + k_{\text{cat}})C, \\ \frac{dP}{dt} &= k_{\text{cat}}C, \end{aligned} \quad (23)$$

where  $S$ ,  $C$ ,  $P$  and  $E$  now represent the *concentrations* of the various reactants. Note that this system has only two degrees of freedom due to conservation relations  $E+C = E_0$  and  $S+C+P = S_0$ , where  $E_0$  and  $S_0$  are the initial concentrations of the enzyme and substrate, respectively. If  $k_f, k_r \gg k_{\text{cat}}$  we might approximate the concentration of the complex  $C$  by the equilibrium value it would have if  $k_{\text{cat}}$  were actually zero:

$$k_f ES - k_r C \approx 0 \quad \Rightarrow \quad C \approx E_0 \frac{S}{k + S}, \quad (24)$$

where  $k = k_r/k_f$ . Introducing  $v^* = k_{\text{cat}}E_0$ , on the slower timescale the net production rate is then found to be

$$\frac{dP}{dt} = \frac{v^* S}{k + S}. \quad (25)$$

This is the Michaelis-Menten law.

In finite volume domains chemical reactions are subject to random fluctuations arising from the discrete nature of the molecules involved. A more appropriate description in these circumstances is a stochastic differential equation, with noise terms that are derived from the instantaneous reaction rates (each possible reaction introduces its own source of noise). For the reaction described above

in (22) occurring in a domain of volume  $V$ , equations are derived following Kurtz (Kurtz, 1978)<sup>3</sup>:

$$\begin{aligned}\frac{dS}{dt} &= -k_f(E_0 - C)S + k_rC - \sqrt{\frac{k_f(E_0 - C)S}{V}}\eta_f(t) + \sqrt{\frac{k_rC}{V}}\eta_r(t), \\ \frac{dC}{dt} &= k_f(E_0 - C)S - (k_r + k_{\text{cat}})C + \sqrt{\frac{k_f(E_0 - C)S}{V}}\eta_f(t) - \sqrt{\frac{k_rC}{V}}\eta_r(t) - \sqrt{\frac{k_{\text{cat}}C}{V}}\eta_{\text{cat}}(t).\end{aligned}\tag{26}$$

Following similar lines to (Heineken et al., 1967) a dimensionless form may be found by rescaling time  $t \mapsto k_f E_0 t$  and introducing variables

$$\mathbf{x} = \begin{pmatrix} S/S_0 \\ C/E_0 \end{pmatrix}, \tag{27}$$

and parameters

$$\varepsilon = \frac{k_{\text{cat}}}{k_f E_0} > 0, \quad \mu = \frac{1}{S_0 V}, \quad \alpha = \frac{k_r}{k_f S_0} > 0, \quad \beta = \frac{S_0}{E_0} > 0. \tag{28}$$

The result is a system of exactly the form of equation (1):

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}) + \varepsilon \mathbf{h}(\mathbf{x}) + \sqrt{\mu} \mathbf{G}(\mathbf{x}) \boldsymbol{\eta}(t), \tag{29}$$

where

$$\mathbf{f}(\mathbf{x}) = \begin{pmatrix} -x_1 + (x_1 + \alpha)x_2 \\ \beta(x_1 - (x_1 + \alpha)x_2) \end{pmatrix}, \quad \mathbf{h}(\mathbf{x}) = \begin{pmatrix} 0 \\ -x_2 \end{pmatrix}, \tag{30}$$

and

$$\mathbf{G}(\mathbf{x}) = \begin{pmatrix} -\sqrt{(1-x_2)x_1} & \sqrt{\alpha x_2} & 0 \\ \sqrt{(1-x_2)x_1} & -\sqrt{\alpha x_2} & -\sqrt{\varepsilon \beta x_2} \end{pmatrix}, \quad \boldsymbol{\eta}(t) = \begin{pmatrix} \eta_f(t) \\ \eta_r(t) \\ \eta_{\text{cat}}(t) \end{pmatrix}. \tag{31}$$

The slow manifold in this case is the curve  $x_1 - x_2(x_1 + \alpha) = 0$ , along which  $\mathbf{f}(\mathbf{x}) = \mathbf{0}$ . See Figure 1 for an illustration.

Let us take  $z = x_1$  as the slow variable and proceed to calculate a reduced system in terms of  $z$  only. As the manifold is one-dimensional, we are able to simply follow the procedure laid out above. We begin by writing down the formula for the slow manifold and its  $z$  derivatives:

$$\boldsymbol{\gamma}(z) = \begin{pmatrix} z \\ \frac{z}{z+\alpha} \end{pmatrix} \quad \boldsymbol{\gamma}'(z) = \begin{pmatrix} 1 \\ \frac{\alpha}{(z+\alpha)^2} \end{pmatrix} \quad \boldsymbol{\gamma}''(z) = \begin{pmatrix} 0 \\ \frac{-2\alpha}{(z+\alpha)^3} \end{pmatrix}. \tag{32}$$

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<sup>3</sup> In fact this step is not strictly necessary; we could choose to work directly with the process of particle numbers, as described in Section IV.C.

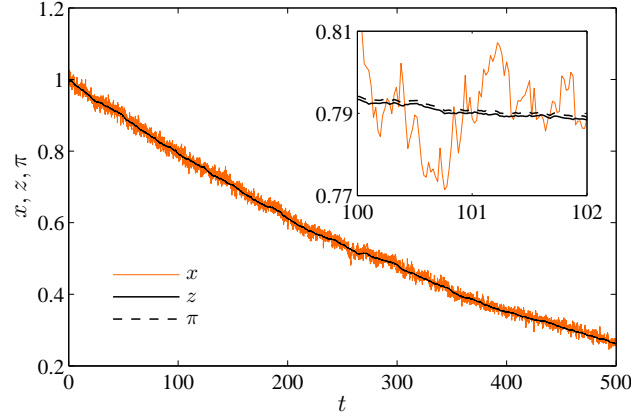


FIG. 4 Trajectories of  $x_1$ ,  $z$  and  $\pi_1(\mathbf{x})$  from a single stochastic simulation of the Michaelis-Menten model. Note that the reduced dimension model for  $z$  given by equation (37) captures the dynamics of the full system under the projection  $\pi$  (hence the extremely close agreement between the solid and dashed black lines above). The original coordinate  $x_1$  is subject to additional noise in the kernel of the projection.

Next, we find the Jacobian matrix on the manifold

$$\mathbf{J}(\mathbf{x}) = \begin{pmatrix} x_2 - 1 & x_1 + \alpha \\ \beta(1 - x_2) & -\beta(x_1 + \alpha) \end{pmatrix} \Rightarrow \mathbf{J}(z) = \begin{pmatrix} \frac{z}{z+\alpha} - 1 & z + \alpha \\ \beta(1 - \frac{z}{z+\alpha}) & -\beta(z + \alpha) \end{pmatrix}. \quad (33)$$

Diagonalizing  $\mathbf{J}(z)$  we find the left eigenvector  $\mathbf{v}(z)$  corresponding to the eigenvalue zero, and its  $z$  derivative:

$$\mathbf{v}(z) = \begin{pmatrix} \beta \\ 1 \end{pmatrix} \quad \mathbf{v}'(z) = \begin{pmatrix} 0 \\ 0 \end{pmatrix}. \quad (34)$$

Following equation (15) we obtain

$$\mathbf{P}_{1*}(z) = \frac{(z + \alpha)^2}{\alpha + \beta(z + \alpha)^2} \begin{pmatrix} \beta & 1 \end{pmatrix}, \quad (35)$$

and from equation (16)

$$\mathbf{Q}_{1**}(z) = 2\alpha \left( \frac{(z + \alpha)}{\alpha + \beta(z + \alpha)^2} \right)^3 \begin{pmatrix} \beta^2 & \beta \\ \beta & 1 \end{pmatrix}. \quad (36)$$

Plugging these results into the general formula (8) gives the reduced model

$$\frac{dz}{dt} = -\varepsilon \frac{z(z + \alpha)}{\alpha + \beta(z + \alpha)^2} + \varepsilon \mu \frac{\alpha \beta z (z + \alpha)^2}{(\alpha + \beta(z + \alpha)^2)^2} - \frac{(z + \alpha)^2}{\alpha + \beta(z + \alpha)^2} \sqrt{\varepsilon \mu \frac{\beta z}{z + \alpha}} \eta_{\text{cat}}(t). \quad (37)$$

Notice that there is a positive noise-induced drift term, meaning that the rate of decrease of  $z$  is slowed by the noise. Figure 4 shows the dynamics of  $z$  compared with those of  $x_1$  in the full system for a single realization of the noise.

At first sight equation (37) is considerably more complex than the traditional Michaelis-Menten law, however, carefully transforming back to the original coordinates, one finds the simple result

$$\frac{dP}{dt} = \frac{v^*S}{k+S} + \sqrt{\frac{v^*S}{V(k+S)}} \eta_{\text{cat}}(t). \quad (38)$$

## B. Continuous degrees of freedom: example of competition-limited diffusion

The methods of Section III can readily be extended to infinite dimensional settings. Two recent examples come from work exploring the role of stochasticity in spatial ecological models (Pigolotti and Benzi, 2014; Rogers et al., 2012a). Here we work through a simple illustrative example of diffusing particles coupled by a competitive birth-death interaction; we will show that this competition acts to limit the speed of diffusion of the population. Interested readers are referred to (Etheridge and March, 1991), where the continuum limit of this example has been studied in considerable depth.

Consider the following stochastic process. At time  $t$  there are  $N_t$  individual particles wandering in a one-dimensional space, each following their own Brownian motion with diffusion constant  $D = \sqrt{2\varepsilon}$ . With rate one, each particle may independently ‘reproduce’, creating a daughter particle that initially shares the location of the parent, but thereafter moves independently. Particles ‘die’ with rate proportional to their total number; specifically, the death rate for each particle is  $\mu(N_t-1)$ . We assume the constants  $\mu$  and  $\varepsilon$  are small, but of the same order.

Since the location of the particles does not influence the birth or death rates, it is easy to see that the total number of particles follows a logistic growth law, quickly reaching an equilibrium  $N_t \approx \mu^{-1}$ . The total population size remains at this level while the spatial distribution of particles evolves slowly over a much longer timescale. We are interested in the long-term behaviour of the distribution of particle locations. Introduce the population density

$$u(x) = \mu \sum_{n=1}^{N_t} \delta(x - X_n(t)), \quad (39)$$

where  $X_n$  is the location of particle  $n$  at time  $t$ ,  $\delta$  is the Dirac delta function, and we suppress the dependence of  $u$  on  $t$  to reduce clutter. Simulations suggest that the competitive interaction of the particles limits the extent to which they are able to diffuse away from each other (Figure 5, left panel). This observation can be made quantitative by computing the mean square distance between pairs of particles,

$$\Delta[u] := \mu^2 \sum_{n,m} (X_n(t) - X_m(t))^2 = \iint (x - y)^2 u(x) u(y) dx dy. \quad (40)$$



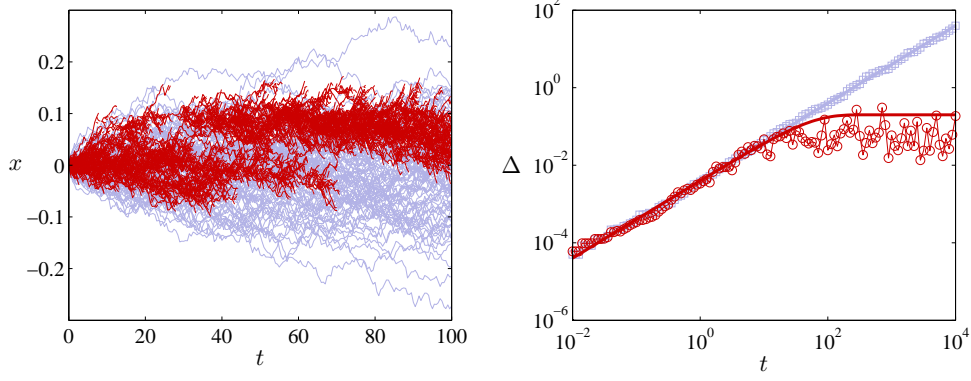


FIG. 5 Simulation of competition-limited diffusion (dark red), contrasted with a collection of  $N$  independent Brownian particles (light purple). The left panel shows the particle trajectories, on the right is shown the mean square distance between pairs of particles.

The right panel of Figure 5 shows the time evolution of  $\Delta$  for the population, compared to the growth  $\Delta \sim t$  observed for independent diffusing particles. The solid lines show our theoretical prediction for this phenomenon, which we will now derive using timescale separation.

Following a system-size expansion (McKane et al., 2014), we find that the time-evolution of  $u(x)$  is described to close approximation by the stochastic partial differential equation (SPDE)

$$\frac{\partial}{\partial t}u(x) = \varepsilon \frac{\partial^2}{\partial x^2}u(x) + u(x) \left(1 - \int u(y) dy\right) + \sqrt{\mu u(x) \left(1 + \int u(y) dy\right)} \eta(x, t), \quad (41)$$

where  $\eta(x, t)$  is spatio-temporal white noise and the integrals run over the real line.

Equation (41) has the same essential structure as our basic object of interest (1). If we identify

$$\begin{aligned} f[u](x) &= u(x) \left(1 - \int u(y) dy\right) \\ h[u](x) &= \frac{\partial^2}{\partial x^2}u(x) \\ G[u](x, s) &= \delta(x - s) \sqrt{u(x) \left(1 + \int u(y) dy\right)}, \end{aligned} \quad (42)$$

then (43) becomes

$$\frac{\partial}{\partial t}u(x) = f[u](x) + \varepsilon h[u](x) + \sqrt{\mu} \int G[u](x, s) \eta(s, t) ds. \quad (43)$$

The integral here is the analogue of the matrix-vector multiplication  $\mathbf{G}(\mathbf{x})\boldsymbol{\eta}(t)$  appearing in (1). The delta function appearing in  $G[u]$  means that the noise in our example is spatially uncorrelated; this may not hold for other models.

In this section we will show how the timescale separation techniques discussed above may also be applied to equations of the form (43). First, an important caveat: the irregular nature of spatio-temporal noise creates enormous mathematical complications in the rigorous analysis of SPDEs,

we refer interested readers to the Fields-medal winning work (Hairer, 2014). In what follows we will turn a blind eye to deeper questions concerning the nature of the solution space and simply apply the techniques developed in the previous sections.

First we examine the outer part  $\partial u / \partial t = f[u]$ . In our example, the PDE

$$\frac{\partial}{\partial t} u(x) = u(x) \left( 1 - \int u(y) dy \right), \quad (44)$$

is straightforward to solve:

$$u(x, t) = \frac{u(x, 0) e^t}{1 + (e^t - 1) \int u(y, 0) dy}, \quad (45)$$

which describes the fast relaxation of  $u$  to a state in which it has total mass one. In this infinite-dimensional setting, the map that describes the long-time limit of the outer solution (previously defined in (5)) is an operator  $\pi$ , whose action is specified by

$$\pi[u](x) = \frac{u(x)}{\int u(y) dy}. \quad (46)$$

We suppose that there exists a suitable space of functions  $\mathcal{U}$  describing possible solutions of (43). Exactly what kind of space is a deep question beyond our present focus. The analogue of the slow manifold is the subspace  $\mathcal{V} \subset \mathcal{U}$  containing functions  $v$  satisfying  $f[v] = 0$ , or equivalently for our example,  $\int v(y) dy = 1$ . We aim to derive an equation describing slow stochastic evolution in  $\mathcal{V}$  that well-approximates the behaviour of solutions to the full system (43).

Where previous calculations involved partial differentiation, we now apply a functional derivative. In analogue to the definitions in (9) we introduce

$$P[v](x, y) = \frac{\delta}{\delta u(y)} \pi[u](x) \Big|_{u=v}, \quad Q[v](x, y, z) = \frac{\delta^2}{\delta u(y) \delta u(z)} \pi[u](x) \Big|_{u=v}. \quad (47)$$

The reduced system may then be written down:

$$\begin{aligned} \frac{\partial}{\partial t} v(x) = & \int P[v](x, y) \left[ \varepsilon h(y) dy + \sqrt{\mu} \int G[v](y, s) \eta(s, t) ds \right] \\ & + \frac{\mu}{2} \iiint G[v](y, s) G[v](z, s) Q[v](x, y, z) dy dz ds. \end{aligned} \quad (48)$$

For the example at hand we compute

$$\begin{aligned} \frac{\delta}{\delta u(y)} \pi[u](x) &= \frac{\delta(x - y)}{\int u(z) dz} - \frac{u(x)}{(\int u(z) dz)^2}, \\ \frac{\delta^2}{\delta u(y)^2} \pi[u](x) &= \frac{2u(x)}{(\int u(z) dz)^3} - \frac{2\delta(x - y)}{(\int u(z) dz)^2}, \end{aligned} \quad (49)$$

and thus

$$P[v](x, y) = \delta(x - y) - v(x), \quad Q[v](x, y, y) = 2v(x) - 2\delta(x - y). \quad (50)$$

Note that we only need the  $z = y$  parts of  $Q[v](x, y, z)$  because of the delta function in  $G$ . Plugging (42) and (50) into (48), we obtain the reduced model

$$\frac{\partial}{\partial t} v(x) = \varepsilon \frac{\partial^2}{\partial x^2} v(x) + \sqrt{2\mu} \int [\delta(x - y) - v(x)] \sqrt{v(y)} \eta(y, t) dy. \quad (51)$$

Comparing (51) to the original equation (41) we see two main differences: the non-linearity in the drift has vanished, but the noise is now spatially coupled.

To compute a prediction for the mean squared distance between particles, it is simpler to work in Fourier space. Introducing  $\tilde{v}(k) = \int e^{-2\pi i k x} v(x) dx$ , we note first that

$$\mathbb{E}\Delta[v] = \iint z^2 e^{2\pi i k z} \mathbb{E}|\tilde{v}(k)|^2 dk dz = -\frac{1}{4\pi^2} \frac{\partial^2}{\partial k^2} \mathbb{E}|\tilde{v}(k)|^2 \Big|_{k=0} \quad (52)$$

Translating (51) to Fourier space we find

$$\frac{\partial}{\partial t} \tilde{v}(k) = -4\varepsilon\pi^2 k^2 \tilde{v}(k) + \sqrt{2\mu} \int \tilde{G}[\tilde{v}](k, x) \eta(x, t) dx, \quad (53)$$

where

$$\tilde{G}[\tilde{v}](k, x) = \left( e^{-2\pi i k x} - \tilde{v}(k) \right) \sqrt{\int e^{2\pi i \ell x} \tilde{v}(\ell) d\ell}. \quad (54)$$

In mean, this process behaves exactly as a straightforward diffusion:

$$\frac{d}{dt} \mathbb{E}[\tilde{v}(k)] = -4\varepsilon\pi^2 k^2 \mathbb{E}[\tilde{v}(k)]. \quad (55)$$

However, the noise introduces a correction to the variance following Itô's formula. Specifically,

$$\begin{aligned} \frac{d}{dt} \mathbb{E}|\tilde{v}(k)|^2 &= -8\varepsilon\pi^2 k^2 \mathbb{E}|\tilde{v}(k)|^2 + \frac{1}{2} \iiint \tilde{G}[\tilde{v}](\ell, x) \tilde{G}[\tilde{v}](m, x) \frac{\delta^2 |\tilde{v}(k)|^2}{\delta \tilde{v}(\ell) \delta \tilde{v}(m)} dx d\ell dm \\ &= -8\varepsilon\pi^2 k^2 \mathbb{E}|\tilde{v}(k)|^2 + 2\mu(1 - \mathbb{E}|\tilde{v}(k)|^2). \end{aligned} \quad (56)$$

Solving (56) and plugging into (52) gives the prediction

$$\mathbb{E}\Delta[v] = \frac{2\varepsilon}{\mu} (1 - e^{-2\mu t}). \quad (57)$$

This result is shown as the dark red curve in Figure 5. In particular, notice that whilst the mean square distance between diffusing particles grows indefinitely, in the competition coupled process it attains a finite limit  $2\varepsilon/\mu$ .

### C. Other noise sources, including jump processes

Above we developed our results in the context of Itô SDEs, however, (Katzenberger, 1991) proved a more general result that allows us to consider a much broader class of noise processes: semimartingales. Semimartingales are the most general class of stochastic processes for which one may define a stochastic integral and stochastic differential equations (Brownian motion is included as a special case). Suitably adapted, most of the familiar results for SDEs and white-noise integrals, including Itô's formula, remain true in the more general setting (Protter, 2004).

To define a semimartingale, we must first make a few auxiliary definitions. A Markov process  $M(t)$  is a *martingale* if

$$\mathbb{E}[M(t)|M(s)] = M(s).$$

A random variable  $\tau$  taking values in  $[0, \infty)$  is a *stopping time* if one can determine if  $\tau < t$  without knowledge of the future beyond  $t$ ; an example of a stopping time is the first time a diffusion started from 0 exits an interval  $[-a, a]$ .  $M(t)$  is a *local martingale* if there is a sequence of stopping times  $\tau_n \rightarrow \infty$  such that  $M(\min\{t, \tau_n\})$  is a martingale for each  $n$ .

A function is *càdlàg* if it is continuous from the right and has left-hand limits at every point.

The *total variation* of a function  $f$  on an interval  $[a, b]$  is

$$V_b^a(f) = \min_{\{t_i\}} \sum_i |f(t_{i+1}) - f(t_i)|,$$

where the minimum is over all partitions  $a = t_0 < t_1 < \dots < t_n = b$  of  $[a, b]$ . A stochastic process  $A(t)$  is of *finite variation* if it is càdlàg and has finite total variation on all intervals  $[a, b]$  (note that  $A(t)$  is allowed to have jump discontinuities).

Finally,  $Z(t)$  is a semimartingale if it may be written as the sum of a local martingale and a finite variation process,

$$Z(t) = M(t) + A(t).$$

Diffusion processes are the prototypical example of semimartingales, but the class is much broader, and includes processes with jumps, such as Lévy processes; *e.g.* if  $N(t)$  is a Poisson process, then  $M(t) = N(t) - t$  is a local martingale and  $A(t) = t$  is of finite variation, so  $N(t)$  is a semimartingale. Integration with respect to a semimartingale is defined analogously to the Stieltjes integral, except that we require the approximating sum to converge in probability, and, as with the Itô integral, the integrand is always evaluated at the left endpoint of each interval in the partition.

More generally, we can define vector and matrix valued martingales, local martingales, finite variation processes and semimartingales,  $\mathbf{M}(t)$ ,  $\mathbf{A}(t)$ , and  $\mathbf{Z}(t)$ , by requiring the components,  $M_i(t)$  *etc.*, have the corresponding property.

We can now formulate Katzenberger's result. Let

(i)  $\mathbf{Z}_n(t)$  be a convergent sequence of vector valued semimartingales such that the jumps  $\Delta \mathbf{Z}_n(t) \rightarrow 0$  as  $n \rightarrow \infty$ ,

(ii)  $A_n(t)$  be a sequence of non-decreasing finite variation processes such that  $\Delta A_n(t) \rightarrow 0$ , and

$$\int_a^b dA_n(s) = A_n(b) - A_n(a) \rightarrow \infty;$$

Katzenberger notes that most frequently in applications,  $A_n(t) = \alpha_n t$  for some sequence  $\alpha_n \rightarrow \infty$  (*n.b.*, in this formulation, this explosion in  $A_n(s)$  corresponds to the drift becoming infinitely strong, rather than the noise infinitely weak, as in (1). The two are equivalent, if one changes the timescale accordingly; recall we had

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}) + \varepsilon \mathbf{h}(\mathbf{x}) + \sqrt{\mu} \mathbf{G}(\mathbf{x}) \boldsymbol{\eta}(t).$$

If instead, we consider the process  $\tilde{\mathbf{x}}(t) = \mathbf{x}(\mu t)$ , we get

$$\frac{d\tilde{\mathbf{x}}}{dt} = \frac{1}{\mu} \mathbf{f}(\tilde{\mathbf{x}}) + \frac{\varepsilon}{\mu} \mathbf{h}(\tilde{\mathbf{x}}) + \mathbf{G}(\tilde{\mathbf{x}}) \boldsymbol{\eta}(t),$$

with a drift that blows up as  $\mu \rightarrow 0$ ).

(iii)  $\mathbf{f}$  and  $\Gamma$  be as before,

(iv)  $\mathbf{G}_n(\mathbf{x})$  be a sequence of matrix-valued functions converging to a limit  $\mathbf{G}(\mathbf{x})$ , and

(v)  $\mathbf{x}_n(t)$  be a sequence of stochastic processes satisfying the (semimartingale) SDE

$$\frac{d\mathbf{x}_n}{dt} = \mathbf{f}(\mathbf{x}_n) \frac{dA_n}{dt} + \mathbf{G}_n(\mathbf{x}_n) \frac{d\mathbf{Z}_n}{dt}.$$

Then, as before, subject to a few technical considerations, as  $n \rightarrow \infty$ ,  $\mathbf{x}_n$  converges to a diffusion process on  $\Gamma$  satisfying

$$\frac{dz}{dt} = \mathbf{g}(z) + \mathbf{P}(z) \mathbf{G}(z) \boldsymbol{\eta}(t), \tag{58}$$

where  $\mathbf{g}$  is as in equation (10) and  $\boldsymbol{\eta}$  is white noise.

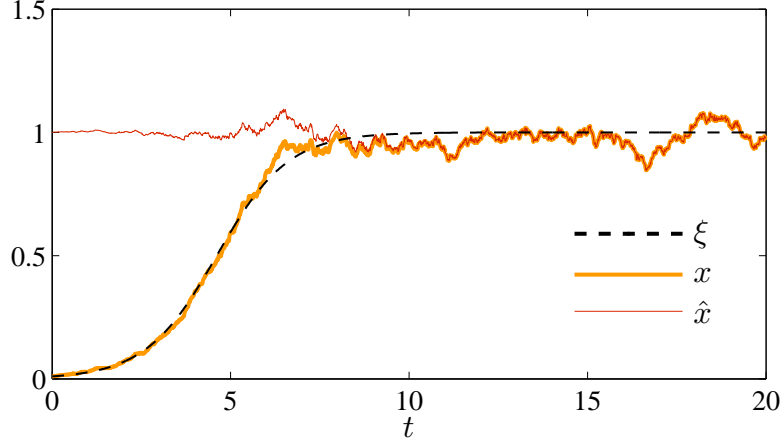


FIG. 6 Illustration of  $\hat{x}_1$  on the fast timescale for a prototypical stochastic dynamical system with a slow manifold  $\Gamma = \{x : x_1 = 1\}$ . In the slow timescale the initial transit to the manifold is compressed into an instantaneous jump at  $t = 0$ .

Some care is required in understanding the sense of convergence in (Katzenberger, 1991); if  $\mathbf{x}_n(0)$  converges weakly to  $\mathbf{z} \in \Gamma$  in  $\mathbb{R}^d$  (*i.e.*, for all continuous functions  $F : \mathbb{R}^d \rightarrow \mathbb{R}$ ,  $\mathbb{E}[F(\mathbf{x}_n(0))] \rightarrow \mathbb{E}[F(\mathbf{z})]$ ) then  $\mathbf{x}_n(t)$  converges weakly to  $\mathbf{z}(t)$  in the space of càdlàg functions:

$$\mathbb{E}[F(\mathbf{x}_n(t))] \rightarrow \mathbb{E}[F(\mathbf{z}(t))]$$

for all continuous functions  $F$  from the space of càdlàg functions on  $[0, \infty)$  to  $\mathbb{R}$ , see (Billingsley, 1968; Ethier and Kurtz, 1986) for a definition of the topology on càdlàg functions and results on weak convergence. When  $\mathbf{x}_n(0)$  converges to a limit  $\mathbf{x}$  that is not in  $\Gamma$ , additional care is required: in this case, the process will jump instantaneously from  $\mathbf{x}$  to  $\boldsymbol{\pi}(\mathbf{x}) \in \Gamma$ , which is not compatible with convergence in the weak topology on càdlàg functions. However, if one considers

$$\hat{\mathbf{x}}_n(t) = \mathbf{x}_n(t) - \boldsymbol{\xi}(nt) + \boldsymbol{\pi}(\mathbf{x}),$$

(recall,  $\boldsymbol{\xi}(t)$  is the solution to the outer system, (4)) then  $\hat{\mathbf{x}}_n(0) \rightarrow \boldsymbol{\pi}(\mathbf{x}) \in \Gamma$  and  $\hat{\mathbf{x}}_n(t)$  converges weakly to the diffusion  $\mathbf{z}(t)$  on  $\Gamma$  as before; intuitively  $\hat{\mathbf{x}}_n(t)$  is obtained by removing the initial transient phase when  $\mathbf{x}_n(t)$  follows the trajectories of the outer system, and starting the process instead from the endpoint of that trajectory,  $\boldsymbol{\pi}(\mathbf{x})$  (see Figure 6).

While Katzenberger's result might seem unnecessarily abstract, it allows one to apply the same slow-manifold reduction to a number of individual-based, discrete stochastic processes that include a number of well-known examples from applications. In (Kurtz, 1970, 1971, 1978, 1981), Kurtz introduced and studied what he called density dependent population processes. While his original

motivation was chemical reaction networks, the class also includes many examples of interest in biology and epidemiology.

A sequence of Markov processes  $\mathbf{x}_n(t)$  is a *density dependent population process* if  $\mathbf{x}_n$  takes values in  $\frac{1}{n}\mathbb{Z}^d$ , and, if  $q_{\mathbf{x},\mathbf{y}}^{(n)}$  is the jump rate between  $\mathbf{x}, \mathbf{y} \in \frac{1}{n}\mathbb{Z}^d$ , then

$$q_{\mathbf{x},\mathbf{y}}^{(n)} = n\lambda_{n(\mathbf{y}-\mathbf{x})}(\mathbf{x})$$

for some non-negative function  $\lambda_{\mathbf{l}}(\mathbf{x})$  on  $\mathbb{R}^d$ , where  $\mathbf{l} = n(\mathbf{y} - \mathbf{x}) \in \mathbb{Z}^d$ . More generally, one can consider the case of functions  $\lambda_{\mathbf{l}}^{(n)}(\mathbf{x})$  that depend on  $n$ , provided  $\lambda_{\mathbf{l}}^{(n)}(\mathbf{x})$  converges to a limit  $\lambda_{\mathbf{l}}(\mathbf{x})$  sufficiently quickly as  $n \rightarrow \infty$ ; see (Pollett, 1990).

The parameter  $n$  corresponds to the “system size” in (van Kampen, 1992), and can be interpreted differently according to the context, as *e.g.* total population size, area, or volume. For example, consider the stochastic logistic process  $X_n(t)$  with birth and death rates

$$Q_{X,X+1}^{(n)} = \beta X \left(1 - \frac{X}{n}\right) \quad Q_{X,X-1}^{(n)} = \delta X.$$

Here,  $n$  plays the role of the carrying capacity in the deterministic logistic equation, *i.e.* the number of individuals the environment can support: individuals have an intrinsic per-capita birth rate  $\beta$ , but the offspring will only survive if it arrives in an unoccupied spot in the habitat. Nondimensionalising, we might consider instead the process  $x_n(t) = \frac{1}{n}X_n(t)$ , with rates

$$q_{x,x+\frac{1}{n}}^{(n)} = n\beta x(1-x) \quad q_{x,x-\frac{1}{n}}^{(n)} = n\delta x.$$

The latter is an example of a density-dependent population process, with

$$\lambda_1(x) = \beta x(1-x) \quad \lambda_{-1}(x) = \delta x.$$

In (Kurtz, 1970), Kurtz shows that provided

$$\sum_{\mathbf{l} \in \mathbb{Z}^d} \|\mathbf{l}\| \sup_{\mathbf{x} \in \mathcal{K}} \lambda_{\mathbf{l}}(\mathbf{x}) < \infty$$

for all closed and bounded sets  $\mathcal{K}$ , then if

$$\mathbf{f}(\mathbf{x}) = \sum_{\mathbf{l} \in \mathbb{Z}^d} \mathbf{l} \lambda_{\mathbf{l}}(\mathbf{x})$$

is differentiable and  $\mathbf{x}_n(t) \rightarrow \mathbf{x}_0$ , then for any fixed  $T > 0$ ,

$$\lim_{n \rightarrow \infty} \sup_{t \leq T} |\mathbf{x}_n(t) - \mathbf{x}(t)| = 0,$$

where  $\mathbf{x}(t)$  is the solution of  $\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x})$  with  $\mathbf{x}(0) = \mathbf{x}_0$ .

If one assumes that  $\lambda_l(\mathbf{x})$  is non-zero for only finitely many transitions, say  $\mathbf{l}_1, \dots, \mathbf{l}_s$ , then, letting  $\mathbf{G}(\mathbf{x})$  be the matrix with  $i^{\text{th}}$  column  $\mathbf{l}_i \sqrt{\lambda_{l_i}(\mathbf{x})}$ ,  $\boldsymbol{\eta}(t)$  be an  $s$ -dimensional Itô white noise, and  $\mathbf{z}_n(t)$  be the solution of

$$\frac{d\mathbf{z}_n}{dt} = \mathbf{f}(\mathbf{z}_n) + \frac{1}{\sqrt{n}} \mathbf{G}(\mathbf{z}_n) \boldsymbol{\eta}(t),$$

then for any fixed  $T > 0$ , there exists a constant  $C_T$  such that

$$\lim_{n \rightarrow \infty} \mathbb{P} \left( \sup_{t \leq T} |\mathbf{x}_n(t) - \mathbf{z}_n(t)| > \frac{C_T \log n}{n} \right) = 0.$$

In our current setting, if  $\mathbf{f}(\mathbf{x})$  is twice continuously differentiable and once again has a globally attractive  $m$ -dimensional manifold of equilibria  $\Gamma$ , then the process  $\mathbf{z}_n(t) = \mathbf{x}_n(nt)$  satisfies the conditions of (Katzenberger, 1991), so that as  $n \rightarrow \infty$ ,  $\mathbf{z}_n(t)$  converges to a diffusion  $\mathbf{z}(t)$  satisfying equation (58) for  $\mathbf{f}$  and  $\mathbf{G}$  defined as above. This result was applied to the study population genetic and epidemiological models in (Parsons, 2012; Parsons et al., 2010).

#### D. Diffusion processes on manifolds

Let  $M$  be a  $m$ -dimensional Riemannian manifold, and, without loss of generality, assume that  $M$  is embedded in  $\mathbb{R}^d$ . Let  $\mathbf{g} = (g_{ij})$  be the metric on  $M$ ; in what follows, we will adopt the convention of writing the entries of  $\mathbf{g}^{-1}$  as  $g^{ij}$ . Let  $\mathbf{p} \in M$  and let  $\mathbf{x}$  be a local chart on  $M$  at  $\mathbf{p}$  *i.e.*  $\mathbf{x}$  is a diffeomorphism from an open neighbourhood  $U$  of  $\mathbf{p}$  in  $M$  to  $\mathbb{R}^m$ , and  $\mathbf{x}(\mathbf{p}) = \mathbf{0}$ . Let  $\mathbf{e}_1, \dots, \mathbf{e}_m$  denote the standard basis on  $\mathbb{R}^m$ . Then, given  $f : M \rightarrow \mathbb{R}$ , we can define the partial derivatives with respect to the  $x_i$  as

$$\left. \frac{\partial f}{\partial x_i} \right|_{\mathbf{p}} = \left. \frac{\partial}{\partial t} \right|_{t=0} f(\mathbf{x}^{-1}(\mathbf{x}(\mathbf{p}) + t\mathbf{e}_i)),$$

and the *Laplace-Beltrami operator* on  $M$ ,  $\nabla_M^2$ , by

$$\nabla_M^2 = \sum_{i,j=1}^d \frac{1}{\sqrt{|\det \mathbf{g}|}} \frac{\partial}{\partial x_i} \left( \sqrt{|\det \mathbf{g}|} g^{ij} \frac{\partial}{\partial x_j} \right).$$

Then, just as white noise has the Laplace equation,

$$\frac{\partial p}{\partial t} = \frac{1}{2} \nabla^2 p,$$

as its' corresponding Fokker-Planck equation, white noise on  $M$ , say  $\boldsymbol{\eta}_M(t)$ , corresponds to the Laplace-Beltrami equation

$$\frac{\partial p}{\partial t} = \frac{1}{2} \nabla_M^2 p.$$



In (Funaki and Nagai, 1993), the authors consider the following variant of (1),

$$\frac{d\mathbf{y}}{dt} = \mathbf{f}(\mathbf{y}) + \sqrt{\mu} \boldsymbol{\eta}_M(t),$$

where  $\mathbf{f}$  is a smooth vector field on  $M$  (*i.e.* for each point  $\mathbf{p} \in M$ ,  $\mathbf{f}(\mathbf{p})$  is a vector in  $T_{\mathbf{p}}M$ , the tangent space to  $M$  at  $\mathbf{p}$ ). They additionally assume that, as before,  $N = \{\mathbf{q} \in M : \mathbf{f}(\mathbf{q}) = \mathbf{0}\}$  is a compact  $m$ -dimensional embedded submanifold of  $M$  without boundary, that  $\frac{d\mathbf{f}}{d\mathbf{x}} = \left(\frac{\partial f_i}{\partial x_j}\right)$  has rank  $d - m$  at every  $\mathbf{q} \in N$  and moreover that every non-zero eigenvalue of  $\frac{d\mathbf{f}}{d\mathbf{x}}$  has negative real part. As previously, the process operates on two time-scales, a fast time in which the process rapidly approaches  $N$  along the flows of  $\mathbf{f}$ , and a slow time in which the time rescaled process  $\mathbf{y}\left(\frac{t}{\mu}\right)$  approaches a diffusion process  $\mathbf{z}(t)$  on  $N$ .

Fundamentally, the approach of (Funaki and Nagai, 1993) and their description of  $\mathbf{z}(t)$  rely on having access to a system of *Fermi coordinates*  $(\mathbf{u}, \mathbf{v})$  defined in a layer about  $N$ . To define these, we first need to introduce a few notions from Riemannian geometry. At each point  $\mathbf{p} \in M$ , the tangent space  $T_{\mathbf{p}}M$  is a vector subspace of  $\mathbb{R}^{d'}$ ; let  $\mathbf{P}(\mathbf{p})$  be the orthogonal projection of  $\mathbb{R}^{d'}$  onto  $T_{\mathbf{p}}M$ . If  $\sigma : \mathbb{R} \rightarrow M$  is a curve taking values in  $M$  and  $\mathbf{g}$  is a vector field on  $M$  then the *covariant derivative* of  $\mathbf{g}$  along  $\sigma$  is

$$\frac{\nabla \mathbf{g}}{dt} = \mathbf{P}(\sigma(t)) \frac{d(\mathbf{g} \circ \sigma)}{dt},$$

and takes values in  $T_{\mathbf{p}}M$ . Given  $\mathbf{p} \in M$  and  $\mathbf{X} \in T_{\mathbf{p}}M$ , there is a unique geodesic curve  $\gamma(t)$  taking values in  $M$  such that  $\gamma(0) = \mathbf{p}$ ,  $\dot{\gamma}(0) = \mathbf{X}$  and such that the covariant derivative of  $\frac{d\gamma}{dt}$  along  $\gamma$  vanishes:

$$\frac{\nabla}{dt} \frac{d\gamma}{dt} = 0.$$

Finally, the *exponential map* at  $\mathbf{p}$ ,  $\text{Exp}_{\mathbf{p}} : T_{\mathbf{p}}M \rightarrow M$  maps  $\mathbf{X} \in T_{\mathbf{p}}M$  to  $\gamma(1)$ , where  $\gamma$  is the geodesic with  $\gamma(0) = \mathbf{p}$  and  $\dot{\gamma}(0) = \mathbf{X}$ .  $\text{Exp}_{\mathbf{p}}$  is a diffeomorphism between a neighbourhood of  $\mathbf{0}$  in  $T_{\mathbf{p}}M$  and a neighbourhood of  $\mathbf{p}$  in  $M$ . To define the Fermi coordinates near a point  $\mathbf{q} \in N$ , one begins with an arbitrary chart  $\mathbf{u}$  on  $N$  and an orthonormal basis  $\mathbf{E}_{m+1}, \dots, \mathbf{E}_n$  of  $(T_{\mathbf{q}}N)^{\perp}$ , the orthogonal complement of  $T_{\mathbf{q}}N$  in  $T_{\mathbf{q}}M$  (as we observed previously for processes in  $\mathbb{R}^d$ ,  $T_{\mathbf{q}}N$  and  $(T_{\mathbf{q}}N)^{\perp}$  are the spaces of slow and fast directions at  $\mathbf{q}$ , respectively). Then, for  $(v_{m+1}, \dots, v_n) \in \mathbb{R}^{d-m}$  sufficiently small,

$$\mathbf{p} = \text{Exp}_{\mathbf{q}} \left( \sum_{j=m+1}^d \eta_j \mathbf{v}_j \right)$$

is a point in  $M$  close to  $N$ , and we define

$$\mathbf{u}(\mathbf{p}) = \mathbf{u}(\mathbf{q}) \quad \text{and} \quad \mathbf{v}(\mathbf{p}) = (v_{m+1}, \dots, v_n).$$

$(\mathbf{u}, \mathbf{v})$  then gives a local chart at  $\mathbf{p}$ . These Fermi coordinates have a number of useful properties:

(i)  $\mathbf{v}(\mathbf{p}) = \mathbf{0}$  if and only if  $\mathbf{p} \in N$ ,

$$(ii) \quad g^{ij}(\mathbf{u}, \mathbf{0}) = \begin{cases} \delta_{ij} & \text{if } i, j > m, \\ 0 & \text{if } i \leq m, j > m, \end{cases}$$

(iii)  $\Gamma_{ij}^k(\mathbf{u}, \mathbf{0}) = 0$  for  $j > m$ , where  $\Gamma_{ij}^k$  are the Christoffel symbols with respect to  $(\mathbf{u}, \mathbf{v})$   
(recall, for a general chart  $\mathbf{x}$  on  $M$ , the Christoffel symbols,

$$\Gamma_{ij}^k = \frac{1}{2} \sum_{l=1}^d g^{kl} \left( \frac{\partial g_{li}}{\partial x_j} - \frac{\partial g_{ij}}{\partial x_l} + \frac{\partial g_{jl}}{\partial x_i} \right),$$

provide corrections to derivatives that account for the curvature of  $M$ ).

$$(iv) \quad \nabla_N f = \sum_{i,j=1}^m g^{ij}(\mathbf{u}, \mathbf{0}) \frac{\partial^2 f}{\partial u_i \partial u_j} - \sum_{k=1}^m g^{jk}(\mathbf{u}, \mathbf{0}) \Gamma_{jk}^i(\mathbf{u}, \mathbf{0}) \frac{\partial f}{\partial u_i}.$$

Having defined  $(\mathbf{u}, \mathbf{v})$ , we can now give the backward equation for  $\mathbf{z}(t)$  from (Funaki and Nagai, 1993): for  $i = 1, \dots, n$  and  $j, k = m+1, \dots, n$ , let

$$A_{ij}(\mathbf{u}) = \frac{\partial f_i}{\partial v_j}(\mathbf{u}, \mathbf{0}),$$

and

$$B_{ijk}(\mathbf{u}) = \frac{\partial^2 f_i}{\partial v_j \partial v_k}(\mathbf{u}, \mathbf{0}),$$

and let  $A$  be the  $(d-m) \times (d-m)$ -matrix  $(A_{ij}(\mathbf{u}))_{i,j=m+1}^d$ . Let  $Y = A^{-1}$ , and

$$Z = \int_0^\infty e^{tA} e^{tA^T} dt,$$

and for  $i \leq m$  and  $j > m$ , let

$$F_{ij}(\mathbf{u}) = \sum_{k=m+1}^d A_{ik}(\mathbf{u}) Y_{kj}(\mathbf{u})$$

and

$$\begin{aligned} G_i(\mathbf{u}) = & \frac{1}{2} \sum_{j,k=m+1}^d B_{ijk}(\mathbf{u}) Z_{jk}(\mathbf{u}) - \frac{1}{2} \sum_{j=m+1}^d \Gamma_{jj}^i(\mathbf{u}, \mathbf{0}) + \frac{1}{2} \sum_{j,k=1}^d \sum_{l=m+1}^d g^{jk}(\mathbf{u}, \mathbf{0}) \Gamma_{jk}^i(\mathbf{u}, \mathbf{0}) F_{il}(\mathbf{u}) \\ & - \frac{1}{2} \sum_{j,k,l=m+1}^d B_{jkl}(\mathbf{u}) Z_{kl}(\mathbf{u}) F_{il}(\mathbf{u}) - \sum_{j=1}^m \sum_{k,l=m+1}^d \left( A_{jk}(\mathbf{u}) Z_{kl}(\mathbf{u}) + \frac{1}{2} F_{jl}(\mathbf{u}) \right) \frac{\partial F_{il}}{\partial u_j}. \end{aligned}$$

Then,  $\mathbf{z}(t)$  has backward equation

$$\frac{\partial p}{\partial t} = \frac{1}{2} \nabla_N^2 p + \frac{1}{2} \sum_{i,j=1}^m \sum_{k=m+1}^d F_{ik} \frac{\partial}{\partial u_i} \left( F_{jk} \frac{\partial p}{\partial u_j} \right) + \sum_{i=1}^m G_i \frac{\partial p}{\partial u_i}.$$

This takes a much simpler form when  $\mathbf{f}$  is a gradient flow on  $M$ . Recall, given a scalar potential  $\phi$  on  $M$ , then in any local chart  $\mathbf{x}$  on  $M$ ,  $\text{grad}_M \phi(\mathbf{p})$  is the vector in  $T_{\mathbf{p}}M$  with  $i^{\text{th}}$  component

$$\sum_{j=1}^d g^{ji}(\mathbf{p}) \frac{\partial f}{\partial x_j} \Big|_{\mathbf{p}}.$$

If  $\mathbf{f} = \text{grad}_M \phi$ , for  $\mathbf{q} \in N$ , let

$$\Phi(\mathbf{q}) = \frac{1}{2} \log \left( \det \left( \frac{\partial^2 \phi}{\partial v_i \partial v_j}(\mathbf{u}(\mathbf{q}), \mathbf{0}) \right)_{i,j=m+1}^d \right).$$

Then, the backward equation for  $\mathbf{z}(t)$  reduces to the elegant

$$\frac{\partial p}{\partial t} = \frac{1}{2} \nabla_N^2 p - \sum_{i=1}^d (\text{grad}_N \Phi)_i \frac{\partial p}{\partial u_i}.$$

## V. DISCUSSION

The purpose of this article has been to show the derivation and application of a systematic framework for dimension reduction in stochastic dynamical systems that exhibit a separation of timescales. The method is exact in the limit of small noise and well-separated slow and fast dynamics, and experimentally found to be valid as an approximation scheme over a sensible parameter range. We have also presented extensions of the method for infinite dimensional systems and processes coupled to general noise sources.

Our analysis rests on some assumptions about the behaviour of the outer system; we have focused here solely on the situation that the deterministic dynamical system defined by  $\mathbf{f}$  possesses a single, connected and globally attractive manifold of fixed points. In some applications more general scenarios may occur, we now briefly discuss two of interest. Some models may exhibit more than one connected manifold of equilibria; in this case the theory developed here will apply locally to trajectories in the basin of attraction of each manifold individually, but further analysis will be necessary to describe the statistics of noise-driven transitions between manifolds. A possibly more exciting direction for further research is the analysis of noisy behaviour around more general attractors such as limit cycles, limit tori and strange attractors. In the case of limit cycles some work exists on stochastic extensions to Floquet theory (Boland et al., 2009), however, this is a

linear description that cannot capture any bias analogous to the noise-induced drift in the slow manifold setting.

Finally, it is worth returning to discuss the motivation for this work. As mentioned earlier, variations of the work of Katzenberger have been independently rediscovered by several groups in recent years, almost all of whom have been interested in questions about the role of noise in ecology and evolution. Historically, many theoretical results in this field have been derived from models that assume for convenience a fixed population size. In the deterministic limit this assumption is not important, but we are now beginning to realise that the inclusion of noise can induce radically different and sometimes unexpected behaviour. Mathematically, this is a consequence of the noise-induced drift term  $\mathbf{g}$  that appears in our equation (2), and more generally of the seemingly endless capacity of Itô's lemma to cause surprise. There have been some tentative explorations of the possible evolutionary and ecological consequences of these effects (Constable and McKane, 2014a; Parsons et al., 2010; Rossberg et al., 2013), but much more is yet to be discovered.

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## Appendix A: Derivation of general procedure for high-dimensional manifolds

First we examine the projection matrix  $\mathbf{P}$ . Consider the outer system

$$\frac{d\boldsymbol{\xi}}{dt} = \mathbf{f}(\boldsymbol{\xi}), \quad \boldsymbol{\xi}(0) = \mathbf{x}, \quad (\text{A1})$$

where  $\mathbf{x}$  lies close to a point  $\mathbf{z}$  on the manifold. Varying the initial conditions yields

$$\frac{d}{dt} \frac{\partial \xi_i}{\partial x_j} = \frac{\partial}{\partial x_j} f_i(\boldsymbol{\xi}) = \sum_k \frac{\partial \xi_k}{\partial x_j} \frac{\partial}{\partial \xi_k} f_i(\boldsymbol{\xi}) = \sum_k J_{ik}(\boldsymbol{\xi}) \frac{\partial \xi_k}{\partial x_j} \approx \sum_k J_{ik}(\mathbf{z}) \frac{\partial \xi_k}{\partial x_j}, \quad (\text{A2})$$

*i.e.*

$$\frac{d}{dt} \frac{\partial \boldsymbol{\xi}}{\partial \mathbf{x}} \approx \mathbf{J}(\mathbf{z}) \frac{\partial \boldsymbol{\xi}}{\partial \mathbf{x}}$$

where  $\mathbf{J}$  is the Jacobian matrix of  $\mathbf{f}$ , and in the final step we have approximated  $\mathbf{f}(\mathbf{x})$  by its linear part near  $\mathbf{x} \approx \mathbf{z}$ . Under this approximation the above equation is linear and admits the solution

$$\frac{\partial \boldsymbol{\xi}}{\partial \mathbf{x}} = e^{t\mathbf{J}(\mathbf{z})}. \quad (\text{A3})$$

From the definitions (5) and (9) we recover  $\mathbf{P}$  by taking the limit of large  $t$ ,

$$\mathbf{P}(\mathbf{z}) = \lim_{t \rightarrow \infty} e^{t\mathbf{J}(\mathbf{z})}. \quad (\text{A4})$$

To compute the limit we consider the action of  $e^{t\mathbf{J}(\mathbf{z})}$  on an eigenvector of the Jacobian<sup>4</sup>. If  $\mathbf{u}_i$  is tangent to the manifold then the corresponding eigenvalue  $\lambda_i$  is zero and so  $e^{t\lambda_i} = 1$  and  $\mathbf{P}(\mathbf{z})$  leaves  $\mathbf{u}_i$  unchanged. Alternatively, if  $\mathbf{u}_i$  corresponds to a direction of fast collapse then its eigenvalue is negative and  $e^{t\lambda_i} \rightarrow 0$ , so  $\mathbf{u}_i$  is annihilated by  $\mathbf{P}(\mathbf{z})$ .

Let  $\mathbf{U} = (\mathbf{u}_1, \dots, \mathbf{u}_m)$  be a basis of the tangent plane to the manifold at  $\mathbf{z}$  (the slow subspace) and let  $\mathbf{V} = (\mathbf{v}_1, \dots, \mathbf{v}_m)$  a basis of the orthogonal complement of the fast subspace. Then we may write

$$\mathbf{P}(\mathbf{z}) = \mathbf{U}(\mathbf{V}^T \mathbf{U})^{-1} \mathbf{V}^T. \quad (\text{A5})$$

In the above we assumed that the tangent plane to the manifold was precisely the kernel of the Jacobian, in which case  $\mathbf{U}$  would be the first  $m$  columns of the right eigenvector matrix, and  $\mathbf{V}^T$  the bottom  $d - m$  rows of the left eigenvector matrix. This may not hold if the manifold is not hyperbolic (for example if  $\mathbf{f}$  has a component like  $-x_i^3$ , which is stable but not linearly so), however, equation (A5) remains true for all flow fields, provided we somehow have access to bases  $\mathbf{U}$  and  $\mathbf{V}$ .

Let us move on to calculate  $\mathbf{Q}$ . We start by obtaining some simple identities: first note that by the definition of  $\boldsymbol{\pi}$ , we have  $f_i(\boldsymbol{\pi}(\mathbf{x})) = 0$  for all  $\mathbf{x}$ . Differentiating this, we obtain

$$\sum_m \frac{\partial f_i}{\partial x_m}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial \pi_m}{\partial x_j} = 0, \quad (\text{A6})$$

or, in matrix form,  $\mathbf{J}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}} = \mathbf{0}$ . Replacing  $\mathbf{x}$  by  $\mathbf{z} \in \Gamma$ , and recalling that  $\frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}}(\mathbf{z}) = \mathbf{P}(\mathbf{z})$ , we have

$$\mathbf{J}(\mathbf{z})\mathbf{P}(\mathbf{z}) = \mathbf{0},$$

---

<sup>4</sup> To simplify the discussion we assume that  $\mathbf{J}(\mathbf{z})$  is diagonalizable and that its kernel contains only the tangent plane to the manifold. Neither assumption is necessary.

*i.e.*  $\mathbf{J}(\mathbf{z})$  annihilates all the slow directions, as we have already observed. Differentiating (A6), we obtain

$$\sum_{m,n} \frac{\partial^2 f_i}{\partial x_m \partial x_n}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial \pi_m}{\partial x_j} \frac{\partial \pi_n}{\partial x_k} + \sum_m \frac{\partial f_i}{\partial x_m}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial^2 \pi_m}{\partial x_j \partial x_k} = 0,$$

which we can write in vector form as

$$\mathcal{H}_{jk} \left( \frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}} \right) + \mathbf{J}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial^2 \boldsymbol{\pi}}{\partial x_j \partial x_k} = 0, \quad (\text{A7})$$

where, for any  $n \times n$ -matrix  $A$ ,  $\mathcal{H}_{jk}(A)$  is the vector with  $i^{\text{th}}$  entry

$$\mathcal{H}_{ijk}(A) = \mathbf{e}_j^T A^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2} A \mathbf{e}_k,$$

where  $\mathbf{e}_j$  is the  $j^{\text{th}}$  standard basis vector, and we have written  $\frac{\partial^2 f_i}{\partial \mathbf{x}^2}$  for the Hessian matrix with  $j, k^{\text{th}}$  entry  $\frac{\partial^2 f_i}{\partial x_j \partial x_k}$ . *i.e.*, since  $\frac{\partial \boldsymbol{\pi}}{\partial x_j} = \frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}} \mathbf{e}_j$ ,

$$\mathcal{H}_{ijk} \left( \frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}} \right) = \left( \frac{\partial \boldsymbol{\pi}}{\partial x_j} \right)^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2} \frac{\partial \boldsymbol{\pi}}{\partial x_k} = \sum_{m,n} \frac{\partial^2 f_i}{\partial x_m \partial x_n}(\boldsymbol{\pi}(\mathbf{x})) \frac{\partial \pi_m}{\partial x_j} \frac{\partial \pi_n}{\partial x_k}.$$

Now, recalling that at  $\mathbf{z} \in \Gamma$ ,  $\boldsymbol{\pi}(\mathbf{z}) = \mathbf{z}$ ,  $\frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}} = \mathbf{P}(\mathbf{z})$ , and  $\frac{\partial^2 \pi_i}{\partial x_j \partial x_k}(\mathbf{z}) = Q_{ijk}(\mathbf{z})$ , we can write (A7) as

$$\mathbf{J}(\mathbf{z}) \mathbf{Q}_{jk}(\mathbf{z}) = -\mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})), \quad (\text{A8})$$

where we continue with the convention that  $\mathbf{Q}_{jk}(\mathbf{z})$  is the vector with  $i^{\text{th}}$  entry  $Q_{ijk}(\mathbf{z})$ . Applying  $\mathbf{P}(\mathbf{z})$  to both sides of (A8) gives

$$\mathbf{P}(\mathbf{z}) \mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})) = \mathbf{0}$$

so we see  $\mathcal{H}_{jk}(\mathbf{P}(\mathbf{z}))$  is entirely contained in the eigenspace of fast directions. Notice that restricted to the fast subspace,  $\mathbf{J}(\mathbf{z})$  is a full-rank operator, so that, *restricted to the fast subspace*, (A8) has a unique solution, which we will write as

$$-\mathbf{J}(\mathbf{z})^+ \mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})).$$

( $\mathbf{J}(\mathbf{z})^+$  is an example of a pseudo-inverse:  $\mathbf{J}(\mathbf{z})$  is not invertible, but we can compute the matrix  $\mathbf{J}(\mathbf{z})^+$  which acts as the inverse of  $\mathbf{J}(\mathbf{z})$  when restricted to the fast directions and which annihilates all vectors in the slow directions.) However, on all of  $\mathbb{R}^d$ , the solution to (A8) is not unique, but rather takes the form

$$\mathbf{Q}_{jk}(\mathbf{z}) = -\mathbf{J}(\mathbf{z})^+ \mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})) + \mathbf{S}_{jk}(\mathbf{z})$$

for some vector  $\mathbf{S}_{jk}(\mathbf{z})$  in the slow directions.

To obtain  $\mathbf{S}_{jk}(\mathbf{z})$ , we proceed as we did to obtain  $\mathbf{P}(\mathbf{z})$ , differentiating (A2) to obtain

$$\frac{d}{dt} \frac{\partial^2 \xi_i}{\partial x_j \partial x_k} = \sum_l \mathbf{J}_{il}(\boldsymbol{\xi}) \frac{\partial^2 \xi_l}{\partial x_j \partial x_k} \sum_{m,n} \frac{\partial^2 f_i}{\partial x_m \partial x_n}(\boldsymbol{\xi}) \frac{\partial \xi_m}{\partial x_j} \frac{\partial \xi_n}{\partial x_k}$$

which again write in vector form as

$$\frac{d}{dt} \frac{\partial^2 \boldsymbol{\xi}}{\partial x_j \partial x_k} = \mathbf{J}(\boldsymbol{\xi}) \frac{\partial^2 \boldsymbol{\xi}}{\partial x_j \partial x_k} + \boldsymbol{\mathcal{H}}_{jk} \left( \frac{\partial \boldsymbol{\xi}}{\partial \mathbf{x}} \right). \quad (\text{A9})$$

This may be formally solved by Duhamel's principle to give

$$\frac{\partial^2 \boldsymbol{\xi}}{\partial x_j \partial x_k} = \int_0^t \boldsymbol{\Pi}(s, t) \boldsymbol{\mathcal{H}}_{jk} \left( \frac{\partial \boldsymbol{\xi}}{\partial \mathbf{x}}(x, s) \right) ds$$

where  $\boldsymbol{\Pi}(s, t)$  is the fundamental matrix solving

$$\frac{d}{dt} \boldsymbol{\Pi}(s, t) = \mathbf{J}(\boldsymbol{\xi}(\mathbf{x}, t)) \boldsymbol{\Pi}(s, t), \quad \boldsymbol{\Pi}(s, s) = I.$$

When  $\mathbf{x}$  is taken to be  $\mathbf{z} \in \Gamma$ , since  $\boldsymbol{\xi}(\mathbf{z}, t) = \mathbf{z}$  for all  $\mathbf{z} \in \Gamma$ , we have

$$\boldsymbol{\Pi}(s, t) = e^{(t-s)\mathbf{J}(\mathbf{z})}.$$

Moreover, in this case,  $\frac{\partial \boldsymbol{\pi}}{\partial \mathbf{x}}(\mathbf{z}, t) = e^{t\mathbf{J}(\mathbf{z})}$ , and the solution to (A9) simplifies to

$$\int_0^t e^{(t-s)\mathbf{J}(\mathbf{z})} \boldsymbol{\mathcal{H}}_{jk} \left( e^{s\mathbf{J}(\mathbf{z})} \right) ds,$$

and, thus,

$$\mathbf{Q}_{jk}(\mathbf{z}) = \lim_{t \rightarrow \infty} \frac{\partial^2 \boldsymbol{\xi}}{\partial x_j \partial x_k} = \lim_{t \rightarrow \infty} \int_0^t e^{(t-s)\mathbf{J}(\mathbf{z})} \boldsymbol{\mathcal{H}}_{jk} \left( e^{s\mathbf{J}(\mathbf{z})} \right) ds.$$

Now,  $e^{t\mathbf{J}(\mathbf{z})} \rightarrow \mathbf{P}(\mathbf{z})$  as  $t \rightarrow \infty$ , and

$$\lim_{t \rightarrow \infty} \boldsymbol{\mathcal{H}}_{jk} \left( e^{t\mathbf{J}(\mathbf{z})} \right) = \boldsymbol{\mathcal{H}}_{jk}(\mathbf{P}(\mathbf{z})),$$

both of which are non-zero, so it is not immediately obvious that the integral above converges.

However, the information we've already obtained allows us to resolve these issues. We start by observing that

$$\mathbf{S}_{jk}(\mathbf{z}) = \mathbf{P}(\mathbf{z}) \mathbf{Q}_{jk}(\mathbf{z}) = \lim_{t \rightarrow \infty} \int_0^t \mathbf{P}(\mathbf{z}) e^{(t-s)\mathbf{J}(\mathbf{z})} \boldsymbol{\mathcal{H}}_{jk} \left( e^{s\mathbf{J}(\mathbf{z})} \right) ds,$$

and, since  $e^{(t-s)\mathbf{J}(\mathbf{z})}$  acts like the identity matrix on the slow directions,  $\mathbf{P}(\mathbf{z}) e^{(t-s)\mathbf{J}(\mathbf{z})} = \mathbf{P}(\mathbf{z})$ , so that

$$\mathbf{S}_{jk}(\mathbf{z}) = \lim_{t \rightarrow \infty} \int_0^t \mathbf{P}(\mathbf{z}) \boldsymbol{\mathcal{H}}_{jk} \left( e^{s\mathbf{J}(\mathbf{z})} \right) ds = \mathbf{P}(\mathbf{z}) \int_0^\infty \boldsymbol{\mathcal{H}}_{jk} \left( e^{s\mathbf{J}(\mathbf{z})} \right) ds.$$

Moreover, we've already observed that  $\mathbf{P}(\mathbf{z})\mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})) = \mathbf{0}$ , so

$$\mathbf{S}_{jk}(\mathbf{z}) = \mathbf{P}(\mathbf{z}) \int_0^\infty \mathcal{H}_{jk}(e^{s\mathbf{J}(\mathbf{z})}) - \mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})) ds,$$

and we are left with evaluating the integral

$$\begin{aligned} \int_0^\infty \mathcal{H}_{ijk}(e^{s\mathbf{J}(\mathbf{z})}) - \mathcal{H}_{ijk}(\mathbf{P}(\mathbf{z})) ds &= \int_0^\infty \mathbf{e}_j^T e^{s\mathbf{J}(\mathbf{z})^T} \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) e^{s\mathbf{J}(\mathbf{z})} \mathbf{e}_k - \mathbf{e}_j^T \mathbf{P}(\mathbf{z})^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) \mathbf{P}(\mathbf{z}) \mathbf{e}_k \\ &= \mathbf{e}_j^T \left( \int_0^\infty e^{s\mathbf{J}(\mathbf{z})^T} \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) \mathbf{P}(\mathbf{z}) ds \right) \mathbf{e}_k. \end{aligned}$$

Now,

$$\begin{aligned} &\int_0^\infty e^{s\mathbf{J}(\mathbf{z})^T} \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) \mathbf{P}(\mathbf{z}) ds \\ &= \int_0^\infty (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z}))^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})) ds \\ &\quad + \int_0^\infty (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z}))^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) \mathbf{P}(\mathbf{z}) ds + \int_0^\infty \mathbf{P}(\mathbf{z})^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})) ds, \end{aligned}$$

and, since  $e^{t\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})$  vanishes on the slow directions, and acts as  $e^{t\mathbf{J}(\mathbf{z})}$  restricted to the fast directions,

$$\int_0^\infty e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z}) ds = -\mathbf{J}(\mathbf{z})^+$$

whereas

$$\mathbf{X}_i(\mathbf{z}) = \int_0^\infty (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z}))^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z}) (e^{s\mathbf{J}(\mathbf{z})} - \mathbf{P}(\mathbf{z})) ds$$

is the unique solution to the Lyapunov equation

$$\mathbf{J}(\mathbf{z})^T \mathbf{X}_i(\mathbf{z}) + \mathbf{X}_i(\mathbf{z}) \mathbf{J}(\mathbf{z}) = -\frac{\partial^2 f_i}{\partial \mathbf{x}^2}(\mathbf{z})$$

in the fast subspace (Bellman, 1995). Thus,

$$\mathbf{S}_{jk}(\mathbf{z}) = \mathbf{P}(\mathbf{z}) \tilde{\mathbf{S}}_{jk}(\mathbf{z}),$$

where

$$\tilde{\mathbf{S}}_{ijk}(\mathbf{z}) = \mathbf{e}_j^T \left( \mathbf{X}_i(\mathbf{z}) - (\mathbf{J}(\mathbf{z})^+)^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2} \mathbf{P}(\mathbf{z}) - \mathbf{P}(\mathbf{z})^T \frac{\partial^2 f_i}{\partial \mathbf{x}^2} \mathbf{J}(\mathbf{z})^+ \right) \mathbf{e}_k$$

and, finally,

$$\mathbf{Q}_{jk}(\mathbf{z}) = -\mathbf{J}(\mathbf{z})^+ \mathcal{H}_{jk}(\mathbf{P}(\mathbf{z})) + \mathbf{P}(\mathbf{z}) \tilde{\mathbf{S}}_{jk}(\mathbf{z}).$$



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